BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

GenCore version 5.1.3

OM protein - protein search, using sw model

Run on: November 19, 2002, 17:32:44 ; Search time 86.2973 Seconds
(without alignments)
318.082 Million cell updates/sec

Title: PCT-US02-27145-2
Perfect score: 1048
Sequence: 1 MAEDADMRNELEEMQRRADQ.....SNKTRIDEANQRATKMLGSG 206

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_101002:*
1: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1980.DAT:*
2: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1981.DAT:*
3: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1982.DAT:*
4: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1983.DAT:*
5: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1984.DAT:*
6: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1985.DAT:*
7: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1986.DAT:*
8: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1987.DAT:*
9: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:*
10: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1989.DAT:*
11: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1990.DAT:*
12: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1991.DAT:*
13: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1992.DAT:*
14: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:*
15: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1994.DAT:*
16: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1995.DAT:*
17: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1996.DAT:*
18: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:*
19: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1998.DAT:*
20: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1999.DAT:*
21: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:*
22: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:*
23: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1048	100.0	206	18	AAW30103	Synaptosomal assoc
2	1048	100.0	206	19	AAW79198	Mouse SNAP-25 poly
3	1048	100.0	206	19	AAW43426	Mouse synaptosomal
4	1048	100.0	206	22	AAU00246	Synaptosomal-assoc
5	1048	100.0	206	22	AAU00253	SNARE homologue, s
6	1043	99.5	206	22	AAU02640	Synaptosomal-assoc
7	1042	99.4	206	22	AAU00259	Synaptosomal-assoc
8	1042	99.4	206	22	AAU00260	Synaptosomal-assoc
9	1042	99.4	206	22	AAU00261	Synaptosomal-assoc
10	1042	99.4	206	22	AAU02638	Synaptosomal-assoc
11	1041	99.3	206	22	AAU00262	Synaptosomal-assoc
12	1039	99.1	206	22	AAU00257	Synaptosomal-assoc
13	1039	99.1	206	22	AAU00266	Synaptosomal-assoc
14	1037	99.0	206	22	AAU02171	Synaptosomal-assoc
15	1036	98.9	206	22	AAU00256	Synaptosomal-assoc
16	1036	98.9	206	22	AAU02639	Synaptosomal-assoc
17	1033	98.6	206	22	AAU00258	Synaptosomal-assoc
18	1026	97.9	203	22	AAU02636	Synaptosomal-assoc
19	1022	97.5	202	22	AAU00265	Synaptosomal-assoc
20	1017	97.0	201	22	AAU02637	Synaptosomal-assoc
21	1012	96.6	200	22	AAU00264	Synaptosomal-assoc
22	1009	96.3	198	22	AAU00255	Synaptosomal-assoc
23	1007	96.1	199	22	AAU00263	Synaptosomal-assoc
24	1004	95.8	206	22	AAU00252	SNARE homologue, s
25	625.5	59.7	212	22	ABB64447	Drosophila melanog
26	613.5	58.5	211	22	ABG02947	Novel human diagno
27	613.5	58.5	211	22	AAU00251	SNARE homologue, s
28	609.5	58.2	213	21	AAB57140	Human prostate can
29	587	56.0	116	23	AAO15165	Clostridial neurot
30	581	55.4	116	23	AAO15166	Clostridial neurot
31	451	43.0	106	21	AAG03825	Human secreted pro
32	451	43.0	106	21	AAG03826	Human secreted pro
33	403	38.5	86	22	AAB15584	Human SNAP-25 N-te
34	391.5	37.4	82	22	AAB15581	Human SNAP-25 N-te
35	361.5	34.5	129	21	AAB53705	Human colon cancer
36	353	33.7	70	17	AAR86823	SNAP-25 residues 1
37	310	29.6	64	21	AAG00764	Human secreted pro
38	253	24.1	513	21	AAG32996	Arabidopsis thalia
39	253	24.1	546	21	AAG32995	Arabidopsis thalia
40	253	24.1	714	21	AAG32994	Arabidopsis thalia
41	244	23.3	49	22	AAM57386	Human brain expres
42	230	21.9	247	21	AAG09027	Arabidopsis thalia
43	230	21.9	247	21	AAG23785	Arabidopsis thalia
44	230	21.9	247	21	AAG39336	Arabidopsis thalia
45	230	21.9	270	21	AAG23784	Arabidopsis thalia

ALIGNMENTS

RESULT 1
AAW30103
ID AAW30103 standard; peptide; 206 AA.
XX
AC AAW30103;
XX
DT 06-APR-1998 (first entry)
XX
DE Synaptosomal associated protein.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle

PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Disclosure; Page 27-28; 61pp; English.
XX
CC This sequence represents the human 25 kD synaptosomal associated protein
CC (SNAP-25), which is an inhibitory agent of the invention. The agents of
CC the invention inhibit secretion of neurotransmitter from neuronal cells
CC and is an excitation-secretory uncoupling peptide (I) of at least 20
CC amino acids (aa) all of which correspond substantially to any one of
CC AAW30097-W30102, or more generally any (I) that inhibits 50% of
CC catecholamine secretion from bovine chromaffin cells at a concentration
CC of 10 microM, especially 0.25 microM, or less. (I) are used, as a
CC replacement for Clostridium toxin, to inhibit release of
CC neurotransmitters from synaptic vesicles, specifically for reducing
CC muscle spasticity. Also (I) may be labelled to allow in vivo imaging of
CC intracellular distribution of (I). Compounds for delivering the drug to
CC neural cells provide targeted drug delivery, e.g. of substance P to
CC brain tumours for induction of apoptosis. Unlike the neurotoxins, (I) are
CC not toxic or immunogenic and are more readily available. Their
CC therapeutic effect lasts for several days or weeks, so lower doses or
CC less frequent treatments are required.
XX
SQ Sequence 206 AA;

Query Match 100.0%; Score 1048; DB 18; Length 206;
Best Local Similarity 100.0%; Pred. No. 6.7e-91;
Matches 206; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy    181 IMEKADSNKTRIDEANQRATKMLGSG 206
          |||||||||||||||||||||||||
Db    181 IMEKADSNKTRIDEANQRATKMLGSG 206
```

RESULT 2
AAW79198
ID AAW79198 standard; Protein; 206 AA.
XX
AC AAW79198;
XX
DT 25-NOV-1998 (first entry)
XX
DE Mouse SNAP-25 polypeptide.
XX
KW Hrs-2 polypeptide; ATP-preferring nucleotidase; SNAP-25; vesicle docking;
KW calcium-regulated secretion; secretory vesicle; secretory process; brain;
KW neurotransmitter release; presynaptic membrane; CNS disorder; depression;
KW Parkinson's disease; endocrine system; hormonal imbalance; cell division;
KW thought disorder; schizophrenia; degenerative disorder; anaesthesia; rat;
KW immune system; antigen processing; immunomodulator; viral processing;
KW central nervous system; vesicular release; affective disorder; human;
KW anti-tumour application; membrane trafficking regulation; mouse.
XX
OS Mus sp.
XX
PN WO9838210-A2.
XX
PD 03-SEP-1998.
XX
PF 26-FEB-1998; 98WO-US03789.
XX
PR 26-FEB-1997; 97US-0039159.
XX
PA (STRD) UNIV LELAND STANFORD JUNIOR.
XX
PI Bean AJ, Scheller RH;
XX
DR WPI; 1998-481140/41.
DR N-PSDB; AAV57558.
XX
PT New isolated Hrs-2 nucleotidase - used in assays to identify
PT compounds capable of modulating calcium-regulatory secretion of
PT secretory vesicles, such as in neurotransmitter release
XX
PS Claim 16; Pages 42-44; 55pp; English.
XX
CC This represents a mouse SNAP-25 polypeptide, a component of the protein
CC polypeptides thought to underlie vesicle docking and fusion. The
CC invention provides rat and human Hrs-2 polypeptides which are ATP-
CC preferring nucleotidase that associate with SNAP-25. For identifying a
CC compound capable of modulating calcium-regulated secretion of secretory
CC vesicles, a SNAP-25 polypeptide can be contacted with a Hrs-2
CC polypeptide, in the presence and absence of a test compound. The effect
CC of the test compound on the extent of binding between the SNAP-25 and
CC Hrs-2 polypeptides are measured and a compound is identified as effective
CC if its measured effect on the extent of binding is above a threshold
CC level. The products can be used for identifying drugs capable of
CC affecting secretory processes, such as neurotransmitter release at the
CC active zones of presynaptic membranes. Such drugs can be used for
CC treating disorders or conditions of the central nervous system by
CC selectively enhancing or inhibiting vesicular release in specific areas
CC of the brain, including affective disorders (e.g. depression), disorders
CC of thought (e.g. schizophrenia) and degenerative disorders (Parkinson's
CC disease), as well as applications such as anaesthesia. The drugs can
CC also be used therapeutically in other systems such as the endocrine
CC system for treatment of hormonal imbalances, the immune system for
CC intervention in antigen processing, secreted immunomodulators, and viral
CC processing, as well as anti-tumour applications, such as regulation of
CC membrane trafficking during rapid cell division.
XX
SQ Sequence 206 AA;

Query Match 100.0%; Score 1048; DB 19; Length 206;
Best Local Similarity 100.0%; Pred. No. 6.7e-91;
Matches 206; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy    181 IMEKADSNKTRIDEANQRATKMLGSG 206
          |||||||||||||||||||||||||
Db    181 IMEKADSNKTRIDEANQRATKMLGSG 206
```

RESULT 3
AAW43426
ID AAW43426 standard; Protein; 206 AA.
XX
AC AAW43426;
XX
DT 27-APR-1998 (first entry)
XX
DE Mouse synaptosomal-associated protein-25.
XX
KW Binding domain; mouse; syntaxin; synaptosomal-associated protein; CNS;
KW neurotransmitter; presynaptic membrane; central nervous system; tumour;

GenCore version 5.1.3
Copyright (c) 1993 - 2002 Compugen Ltd.

OM protein - protein search, using sw model

Run on: November 19, 2002, 17:32:44 ; Search time 3.35135 Seconds
(without alignments)
318.082 Million cell updates/sec

Title: PCT-US02-27145-1
Perfect score: 39
Sequence: 1 EANQRATK 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_101002:*
1: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1980.DAT:*
2: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1981.DAT:*
3: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1982.DAT:*
4: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1983.DAT:*
5: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1984.DAT:*
6: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1985.DAT:*
7: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1986.DAT:*
8: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1987.DAT:*
9: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:*
10: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1989.DAT:*
11: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1990.DAT:*
12: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1991.DAT:*
13: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1992.DAT:*
14: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:*
15: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1994.DAT:*
16: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1995.DAT:*
17: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1996.DAT:*
18: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:*
19: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1998.DAT:*
20: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1999.DAT:*
21: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:*
22: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:*
23: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	39	100.0	12	20	AAY44061	Human SNAP25 (amin
2	39	100.0	15	20	AAY44058	Human SNAP25 (amin
3	39	100.0	16	20	AAY44069	Human SNAP25 (amin
4	39	100.0	17	20	AAY44021	Amino acids 187-20
5	39	100.0	17	20	AAY44039	Human SNAP25 (amin
6	39	100.0	17	20	AAY44044	Human SNAP25 (amin
7	39	100.0	17	20	AAY44048	Human SNAP25 (amin
8	39	100.0	17	20	AAY44056	Human SNAP25 (amin
9	39	100.0	17	20	AAY44057	Human SNAP25 (amin
10	39	100.0	17	20	AAY44070	Human SNAP25 (amin
11	39	100.0	17	23	ABG69065	Human polypeptide
12	39	100.0	19	22	AAB15586	Human SNAP-25 N-te
13	39	100.0	20	18	AAW30100	Neurotransmitter s
14	39	100.0	26	18	AAW30099	Neurotransmitter s
15	39	100.0	37	18	AAW30097	Neurotransmitter s
16	39	100.0	70	17	AAR86823	SNAP-25 residues 1
17	39	100.0	86	22	AAB15584	Human SNAP-25 N-te
18	39	100.0	116	23	AAO15165	Clostridial neurot
19	39	100.0	206	18	AAW30103	Synaptosomal assoc
20	39	100.0	206	19	AAW79198	Mouse SNAP-25 poly
21	39	100.0	206	19	AAW43426	Mouse synaptosomal
22	39	100.0	206	22	AAU00246	Synaptosomal-assoc
23	39	100.0	206	22	AAU00252	SNARE homologue, s
24	39	100.0	206	22	AAU00253	SNARE homologue, s
25	39	100.0	206	22	AAU02638	Synaptosomal-assoc
26	39	100.0	206	22	AAU02640	Synaptosomal-assoc
27	36	92.3	12	20	AAY44037	Human SNAP25 (amin
28	36	92.3	13	20	AAY44036	Human SNAP25 (amin
29	36	92.3	16	20	AAY44027	Human SNAP25 (amin
30	36	92.3	16	20	AAY44071	Human SNAP25 (amin
31	36	92.3	16	20	AAY44072	Human SNAP25 (amin
32	36	92.3	16	20	AAY44073	Human SNAP25 (amin
33	36	92.3	16	20	AAY44074	Human SNAP25 (amin
34	36	92.3	17	20	AAY44022	Human SNAP25 (amin
35	36	92.3	17	20	AAY44024	Human SNAP25 (amin
36	36	92.3	17	20	AAY44026	Human SNAP25 (amin
37	36	92.3	17	20	AAY44038	Human SNAP25 (amin
38	36	92.3	17	20	AAY44041	Human SNAP25 (amin
39	36	92.3	17	20	AAY44043	Human SNAP25 (amin
40	36	92.3	17	20	AAY44063	Human SNAP25 (amin
41	36	92.3	24	23	AAO15162	Clostridial neurot
42	35	89.7	17	20	AAY44047	Human SNAP25 (amin
43	35	89.7	17	20	AAY44050	Human SNAP25 (amin
44	35	89.7	17	20	AAY44052	Human SNAP25 (amin
45	35	89.7	17	20	AAY44059	Human SNAP25 (amin

ALIGNMENTS

RESULT 1
AAY44061
ID AAY44061 standard; peptide; 12 AA.
XX
AC AAY44061;
XX
DT 18-JAN-2000 (first entry)
XX
DE Human SNAP25 (amino acids 187-203) analogue #40.
XX
KW Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW hydrolysis; amino group.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN US5965699-A
XX
PD 12-OCT-1999.
XX
PF 06-NOV-1996; 96US-0743894.
XX
PR 06-NOV-1996; 96US-0743894.
XX
PA (USSA) US SEC OF ARMY.
XX
PI Bostian KA, Schmidt JJ;
XX
DR WPI; 1999-579939/49.
XX
PT Quantitation of type A botulinum toxin -
XX

PS Disclosure; Column 9-10; 28pp; English.
XX
CC The invention relates to an enzymatic assay for the quantitation of
CC type A botulinum toxin, by determining the proteolytic activity of
CC botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC toxin A has been shown to cleave the synaptosomal neurotransmitter
CC peptide SNAP25 between residues 197-198. The method comprises adding
CC an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC amino acids 187-203 of human SNAP25) to a sample containing the
CC botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC stopping hydrolysis of the peptide at different time points; and
CC measuring the amount of hydrolysis at each time point by combining with a
CC label capable of detecting free amino groups resulting from the
CC hydrolysis. The amount of botulinum toxin A present in the sample is
CC determined by comparing measurements with the amount of label produced
CC from a known concentration of toxin measured under similar conditions.
CC The method is useful for the quantitation of type A botulinum toxin.
XX
SQ Sequence 12 AA;

Query Match 100.0%; Score 39; DB 20; Length 12;
Best Local Similarity 100.0%; Pred. No. 0.066;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EANQRATK 8
||||||||
Db 3 EANQRATK 10

RESULT 2
AAY44058
ID AAY44058 standard; peptide; 15 AA.
XX
AC AAY44058;
XX
DT 18-JAN-2000 (first entry)
XX
DE Human SNAP25 (amino acids 187-203) analogue [1-15].
XX
KW Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW hydrolysis; amino group.
XX
OS Homo sapiens.
XX
PN US5965699-A.
XX
PD 12-OCT-1999.
XX
PF 06-NOV-1996; 96US-0743894.
XX
PR 06-NOV-1996; 96US-0743894.
XX
PA (USSA) US SEC OF ARMY.
XX
PI Bostian KA, Schmidt JJ;
XX
DR WPI; 1999-579939/49.
XX
PT Quantitation of type A botulinum toxin -
XX
PS Disclosure; Column 9; 28pp; English.
XX
CC The invention relates to an enzymatic assay for the quantitation of
CC type A botulinum toxin, by determining the proteolytic activity of
CC botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC toxin A has been shown to cleave the synaptosomal neurotransmitter
CC peptide SNAP25 between residues 197-198. The method comprises adding
CC an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC amino acids 187-203 of human SNAP25) to a sample containing the
CC botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC stopping hydrolysis of the peptide at different time points; and
CC measuring the amount of hydrolysis at each time point by combining with a
CC label capable of detecting free amino groups resulting from the
CC hydrolysis. The amount of botulinum toxin A present in the sample is
CC determined by comparing measurements with the amount of label produced
CC from a known concentration of toxin measured under similar conditions.
CC The method is useful for the quantitation of type A botulinum toxin.
XX
SQ Sequence 15 AA;

Query Match 100.0%; Score 39; DB 20; Length 15;
Best Local Similarity 100.0%; Pred. No. 0.084;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EANQRATK 8
||||||||
Db 8 EANQRATK 15

RESULT 3
AAY44069
ID AAY44069 standard; peptide; 16 AA.
XX
AC AAY44069;
XX
DT 18-JAN-2000 (first entry)
XX
DE Human SNAP25 (amino acids 187-203) analogue [1-16].
XX
KW Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW hydrolysis; amino group.
XX
OS Homo sapiens.
XX
PN US5965699-A.
XX
PD 12-OCT-1999.
XX
PF 06-NOV-1996; 96US-0743894.
XX
PR 06-NOV-1996; 96US-0743894.
XX
PA (USSA) US SEC OF ARMY.
XX
PI Bostian KA, Schmidt JJ;
XX
DR WPI; 1999-579939/49.
XX
PT Quantitation of type A botulinum toxin -
XX
PS Disclosure; Column 13-14; 28pp; English.
XX
CC The invention relates to an enzymatic assay for the quantitation of
CC type A botulinum toxin, by determining the proteolytic activity of
CC botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC toxin A has been shown to cleave the synaptosomal neurotransmitter
CC peptide SNAP25 between residues 197-198. The method comprises adding
CC an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC amino acids 187-203 of human SNAP25) to a sample containing the
CC botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC stopping hydrolysis of the peptide at different time points; and
CC measuring the amount of hydrolysis at each time point by combining with a
CC label capable of detecting free amino groups resulting from the
CC hydrolysis. The amount of botulinum toxin A present in the sample is
CC determined by comparing measurements with the amount of label produced
CC from a known concentration of toxin measured under similar conditions.
CC The method is useful for the quantitation of type A botulinum toxin.
XX
SQ Sequence 16 AA;

Query Match 100.0%; Score 39; DB 20; Length 16;
Best Local Similarity 100.0%; Pred. No. 0.09;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 EANQRATK 8
          ||||||||
Db      8 EANQRATK 15


RESULT 4
AAY44021
ID   AAY44021 standard; peptide; 17 AA.
XX
AC   AAY44021;
XX
DT   18-JAN-2000  (first entry)
XX
DE   Amino acids 187-203 of human SNAP25.
XX
KW   Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW   fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW   hydrolysis; amino group.
XX
OS   Homo sapiens.
XX
PN   US5965699-A.
XX
PD   12-OCT-1999.
XX
PF   06-NOV-1996;   96US-0743894.
XX
PR   06-NOV-1996;   96US-0743894.
XX
PA   (USSA ) US SEC OF ARMY.
XX
PI   Bostian KA,  Schmidt JJ;
XX
DR   WPI; 1999-579939/49.
XX
PT   Quantitation of type A botulinum toxin -
XX
PS   Claim 1; Column 4; 28pp; English.
XX
CC   The invention relates to an enzymatic assay for the quantitation of
CC   type A botulinum toxin, by determining the proteolytic activity of
CC   botulinum neurotoxin type A using fluorescamine detection. The method
CC   comprises adding an analogue (e.g. AAY44022-Y44076) of this peptide
CC   (which represents amino acids 187-203 of the human synaptosomal protein
CC   SNAP25) to a sample containing the botulinum toxin A so that hydrolysis
CC   of the peptide is initiated, then stopping hydrolysis of the peptide at
CC   different time points; and measuring the amount of hydrolysis at each
CC   time point by combining with a label capable of detecting free amino
CC   groups resulting from the hydrolysis. The amount of botulinum toxin A
CC   present in the sample is determined by comparing measurements with the
CC   amount of label produced from a known concentration of toxin measured
CC   under similar conditions. The method is useful for the quantitation of
CC   type A botulinum toxin.
XX
SQ   Sequence   17 AA;

  Query Match             100.0%;  Score 39;  DB 20;  Length 17;
  Best Local Similarity   100.0%;  Pred. No. 0.097;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 EANQRATK 8
          ||||||||
Db      8 EANQRATK 15


RESULT 5
AAY44039
ID   AAY44039 standard; peptide; 17 AA.
XX
AC   AAY44039;
XX
DT   18-JAN-2000  (first entry)
XX
DE   Human SNAP25 (amino acids 187-203) analogue #18.
XX
KW   Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW   fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW   hydrolysis; amino group.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   4
FT                   /label= Abu
XX
PN   US5965699-A.
XX
PD   12-OCT-1999.
XX
PF   06-NOV-1996;   96US-0743894.
XX
PR   06-NOV-1996;   96US-0743894.
XX
PA   (USSA ) US SEC OF ARMY.
XX
PI   Bostian KA,  Schmidt JJ;
XX
DR   WPI; 1999-579939/49.
XX
PT   Quantitation of type A botulinum toxin -
XX
PS   Disclosure; Column 7-8; 28pp; English.
XX
CC   The invention relates to an enzymatic assay for the quantitation of
CC   type A botulinum toxin, by determining the proteolytic activity of
CC   botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC   toxin A has been shown to cleave the synaptosomal neurotransmitter
CC   peptide SNAP25 between residues 197-198. The method comprises adding
CC   an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC   amino acids 187-203 of human SNAP25) to a sample containing the
CC   botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC   stopping hydrolysis of the peptide at different time points; and
CC   measuring the amount of hydrolysis at each time point by combining with a
CC   label capable of detecting free amino groups resulting from the
CC   hydrolysis. The amount of botulinum toxin A present in the sample is
CC   determined by comparing measurements with the amount of label produced
CC   from a known concentration of toxin measured under similar conditions.
CC   The method is useful for the quantitation of type A botulinum toxin.
XX
SQ   Sequence   17 AA;

  Query Match             100.0%;  Score 39;  DB 20;  Length 17;
  Best Local Similarity   100.0%;  Pred. No. 0.097;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 EANQRATK 8
          ||||||||
Db      8 EANQRATK 15


RESULT 6
AAY44044
ID   AAY44044 standard; peptide; 17 AA.
XX
AC   AAY44044;
XX
DT   18-JAN-2000  (first entry)
XX
DE   Human SNAP25 (amino acids 187-203) analogue M16X.
XX
KW   Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW   fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW   hydrolysis; amino group.
XX
OS   Homo sapiens.
```

OS Synthetic.
XX
FH Key Location/Qualifiers
FT Modified-site 16
FT /label= Nle
XX
PN US5965699-A.
XX
PD 12-OCT-1999.
XX
PF 06-NOV-1996; 96US-0743894.
XX
PR 06-NOV-1996; 96US-0743894.
XX
PA (USSA) US SEC OF ARMY.
XX
PI Bostian KA, Schmidt JJ;
XX
DR WPI; 1999-579939/49.
XX
PT Quantitation of type A botulinum toxin -
XX
PS Disclosure; Column 7-8; 28pp; English.
XX
CC The invention relates to an enzymatic assay for the quantitation of
CC type A botulinum toxin, by determining the proteolytic activity of
CC botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC toxin A has been shown to cleave the synaptosomal neurotransmitter
CC peptide SNAP25 between residues 197-198. The method comprises adding
CC an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC amino acids 187-203 of human SNAP25) to a sample containing the
CC botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC stopping hydrolysis of the peptide at different time points; and
CC measuring the amount of hydrolysis at each time point by combining with a
CC label capable of detecting free amino groups resulting from the
CC hydrolysis. The amount of botulinum toxin A present in the sample is
CC determined by comparing measurements with the amount of label produced
CC from a known concentration of toxin measured under similar conditions.
CC The method is useful for the quantitation of type A botulinum toxin.
XX
SQ Sequence 17 AA;

Query Match 100.0%; Score 39; DB 20; Length 17;
Best Local Similarity 100.0%; Pred. No. 0.097;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EANQRATK 8
||||||||
Db 8 EANQRATK 15

RESULT 7
AAY44048
ID AAY44048 standard; peptide; 17 AA.
XX
AC AAY44048;
XX
DT 18-JAN-2000 (first entry)
XX
DE Human SNAP25 (amino acids 187-203) analogue M16A.
XX
KW Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW hydrolysis; amino group.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN US5965699-A.
XX
PD 12-OCT-1999.
XX
PF 06-NOV-1996; 96US-0743894.
XX
PR 06-NOV-1996; 96US-0743894.
XX
PA (USSA) US SEC OF ARMY.
XX
PI Bostian KA, Schmidt JJ;
XX
DR WPI; 1999-579939/49.
XX
PT Quantitation of type A botulinum toxin -
XX
PS Disclosure; Column 9; 28pp; English.
XX
CC The invention relates to an enzymatic assay for the quantitation of
CC type A botulinum toxin, by determining the proteolytic activity of
CC botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC toxin A has been shown to cleave the synaptosomal neurotransmitter
CC peptide SNAP25 between residues 197-198. The method comprises adding
CC an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC amino acids 187-203 of human SNAP25) to a sample containing the
CC botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC stopping hydrolysis of the peptide at different time points; and
CC measuring the amount of hydrolysis at each time point by combining with a
CC label capable of detecting free amino groups resulting from the
CC hydrolysis. The amount of botulinum toxin A present in the sample is
CC determined by comparing measurements with the amount of label produced
CC from a known concentration of toxin measured under similar conditions.
CC The method is useful for the quantitation of type A botulinum toxin.
XX
SQ Sequence 17 AA;

Query Match 100.0%; Score 39; DB 20; Length 17;
Best Local Similarity 100.0%; Pred. No. 0.097;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EANQRATK 8
||||||||
Db 8 EANQRATK 15

RESULT 8
AAY44056
ID AAY44056 standard; peptide; 17 AA.
XX
AC AAY44056;
XX
DT 18-JAN-2000 (first entry)
XX
DE Human SNAP25 (amino acids 187-203) analogue #35.
XX
KW Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW hydrolysis; amino group.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN US5965699-A.
XX
PD 12-OCT-1999.
XX
PF 06-NOV-1996; 96US-0743894.
XX
PR 06-NOV-1996; 96US-0743894.
XX
PA (USSA) US SEC OF ARMY.
XX
PI Bostian KA, Schmidt JJ;
XX
DR WPI; 1999-579939/49.
XX
PT Quantitation of type A botulinum toxin -
XX

```
PS   Disclosure; Column 9; 28pp; English.
XX
CC   The invention relates to an enzymatic assay for the quantitation of
CC   type A botulinum toxin, by determining the proteolytic activity of
CC   botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC   toxin A has been shown to cleave the synaptosomal neurotransmitter
CC   peptide SNAP25 between residues 197-198. The method comprises adding
CC   an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC   amino acids 187-203 of human SNAP25) to a sample containing the
CC   botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC   stopping hydrolysis of the peptide at different time points; and
CC   measuring the amount of hydrolysis at each time point by combining with a
CC   label capable of detecting free amino groups resulting from the
CC   hydrolysis. The amount of botulinum toxin A present in the sample is
CC   determined by comparing measurements with the amount of label produced
CC   from a known concentration of toxin measured under similar conditions.
CC   The method is useful for the quantitation of type A botulinum toxin.
XX
SQ   Sequence   17 AA;

  Query Match             100.0%;  Score 39;  DB 20;  Length 17;
  Best Local Similarity   100.0%;  Pred. No. 0.097;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 EANQRATK 8
           ||||||||
Db       8 EANQRATK 15


RESULT 9
AAY44057
ID   AAY44057 standard; peptide; 17 AA.
XX
AC   AAY44057;
XX
DT   18-JAN-2000  (first entry)
XX
DE   Human SNAP25 (amino acids 187-203) analogue #36.
XX
KW   Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW   fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW   hydrolysis; amino group.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   US5965699-A.
XX
PD   12-OCT-1999.
XX
PF   06-NOV-1996;   96US-0743894.
XX
PR   06-NOV-1996;   96US-0743894.
XX
PA   (USSA ) US SEC OF ARMY.
XX
PI   Bostian KA,  Schmidt JJ;
XX
DR   WPI; 1999-579939/49.
XX
PT   Quantitation of type A botulinum toxin -
XX
PS   Disclosure; Column 9; 28pp; English.
XX
CC   The invention relates to an enzymatic assay for the quantitation of
CC   type A botulinum toxin, by determining the proteolytic activity of
CC   botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC   toxin A has been shown to cleave the synaptosomal neurotransmitter
CC   peptide SNAP25 between residues 197-198. The method comprises adding
CC   an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC   amino acids 187-203 of human SNAP25) to a sample containing the
CC   botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC   stopping hydrolysis of the peptide at different time points; and
CC   measuring the amount of hydrolysis at each time point by combining with a
CC   label capable of detecting free amino groups resulting from the
CC   hydrolysis. The amount of botulinum toxin A present in the sample is
CC   determined by comparing measurements with the amount of label produced
CC   from a known concentration of toxin measured under similar conditions.
CC   The method is useful for the quantitation of type A botulinum toxin.
XX
SQ   Sequence   17 AA;

  Query Match             100.0%;  Score 39;  DB 20;  Length 17;
  Best Local Similarity   100.0%;  Pred. No. 0.097;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 EANQRATK 8
           ||||||||
Db       8 EANQRATK 15


RESULT 10
AAY44070
ID   AAY44070 standard; peptide; 17 AA.
XX
AC   AAY44070;
XX
DT   18-JAN-2000  (first entry)
XX
DE   Human SNAP25 (amino acids 187-203) analogue D7N.
XX
KW   Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW   fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW   hydrolysis; amino group.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   US5965699-A.
XX
PD   12-OCT-1999.
XX
PF   06-NOV-1996;   96US-0743894.
XX
PR   06-NOV-1996;   96US-0743894.
XX
PA   (USSA ) US SEC OF ARMY.
XX
PI   Bostian KA,  Schmidt JJ;
XX
DR   WPI; 1999-579939/49.
XX
PT   Quantitation of type A botulinum toxin -
XX
PS   Disclosure; Column 15; 28pp; English.
XX
CC   The invention relates to an enzymatic assay for the quantitation of
CC   type A botulinum toxin, by determining the proteolytic activity of
CC   botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC   toxin A has been shown to cleave the synaptosomal neurotransmitter
CC   peptide SNAP25 between residues 197-198. The method comprises adding
CC   an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC   amino acids 187-203 of human SNAP25) to a sample containing the
CC   botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC   stopping hydrolysis of the peptide at different time points; and
CC   measuring the amount of hydrolysis at each time point by combining with a
CC   label capable of detecting free amino groups resulting from the
CC   hydrolysis. The amount of botulinum toxin A present in the sample is
CC   determined by comparing measurements with the amount of label produced
CC   from a known concentration of toxin measured under similar conditions.
CC   The method is useful for the quantitation of type A botulinum toxin.
XX
SQ   Sequence   17 AA;

  Query Match             100.0%;  Score 39;  DB 20;  Length 17;
  Best Local Similarity   100.0%;  Pred. No. 0.097;
```

Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 EANQRATK 8
          ||||||||
Db      8 EANQRATK 15
```

RESULT 11
ABG69065
ID ABG69065 standard; Peptide; 17 AA.
XX
AC ABG69065;
XX
DT 07-OCT-2002 (first entry)
XX
DE Human polypeptide C-terminal fragment.
XX
KW Botulinum neurotoxin light chain; BoNT LC; botulism; dystonia; pain;
KW spasticity; ocular motility; facial dyskinesia; stiff-person syndrome;
KW bladder dysfunction; segmental myoclonus; hyperkinetic disorder; human;
KW cosmetic treatment; facial wrinkle; cerebral palsy; analgesic; relaxant;
KW lower motor neuron hyperactivity; autonomic nerve function; muscular;
KW immunostimulant; antibacterial.
XX
OS Homo sapiens.
XX
PN WO200236758-A2.
XX
PD 10-MAY-2002.
XX
PF 06-NOV-2001; 2001WO-US47230.
XX
PR 06-NOV-2000; 2000US-246774P.
PR 20-JUL-2001; 2001US-0910186.
PR 09-AUG-2001; 2001US-311966P.
XX
PA (USSA) US ARMY MEDICAL RES & MATERIAL COMMAND.
XX
PI Smith LA, Jensen M;
XX
DR WPI; 2002-575192/61.
XX
PT Novel nucleic acid molecule encoding botulinum neurotoxin light chain
PT serotype A, useful for producing the neurotoxin for vaccination against
PT botulism, comprises sequence expressible in host other than Clostridium
PT -
XX
PS Example 25; Page 62; 166pp; English.
XX
CC The invention relates to a nucleic acid molecule encoding a botulinum
CC neurotoxin light chain (BoNT LC) serotype A, where the DNA has a sequence
CC that is expressible in a host organism other than Clostridium, or has a
CC total A+T content that is less than about 70% The BoNT LC protein is
CC useful in vaccination against botulism, for eliciting protective immunity
CC in a mammal, for treating dystonias, spasticity, pain, ocular motility,
CC facial dyskinesias, stiff-person syndrome, bladder dysfunction, segmental
CC myoclonus, hyperkinetic disorders, cosmetic treatment of facial wrinkles,
CC conditions characterised by hyperactivity of the lower motor neuron, and
CC to control autonomic nerve function or tiptoe-walking due to stiff
CC muscles common in children with cerebral palsy. The sequences are also
CC useful for screening for botulinum neurotoxin inhibitors. This sequence
CC represents a human polypeptide C-terminal fragment, used in the scope of
CC the invention.
XX
SQ Sequence 17 AA;

Query Match 100.0%; Score 39; DB 23; Length 17;
Best Local Similarity 100.0%; Pred. No. 0.097;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 EANQRATK 8
          ||||||||
Db      8 EANQRATK 15
```

RESULT 12
AAB15586
ID AAB15586 standard; peptide; 19 AA.
XX
AC AAB15586;
XX
DT 02-MAR-2001 (first entry)
XX
DE Human SNAP-25 N-terminal peptide #6.
XX
KW Dermatological; neuroprotective; relaxant; neuronal exocytosis modulator;
KW SNAP-25; synaptosomal-associated protein 25; facial wrinkle; asymmetry;
KW neurodegenerative disorder.
XX
OS Homo sapiens.
XX
PN WO200064932-A1.
XX
PD 02-NOV-2000.
XX
PF 18-FEB-2000; 2000WO-ES00058.
XX
PR 23-APR-1999; 99ES-0000844.
XX
PA (LIPO-) LIPOTEC SA.
XX
PI Blanes Mira MC, Llobregat Hernandez MM, Gil Tebar AI;
PI Fernandez Ballester GJ, Planell Cases RM, Ferrer Montiel AV;
PI Viniegra Bover S, Gutierrez Perez LM, Carbonell Castell T;
PI Perez Paya E;
XX
DR WPI; 2001-007091/01.
XX
PT New peptides containing amino acid sequences from known proteins for
PT treatment of neurological disorders -
XX
PS Claim 17; Page 34; 40pp; Spanish.
XX
CC The invention relates to new peptides comprising 3-30 contiguous amino
CC acids from the N-terminus of the protein SNAP-25
CC (synaptosomal-associated protein 25). The peptides AAB15581-B15586
CC represent examples of the peptides of the invention. The peptides have
CC neuronal exocytosis inhibitory activity and are used for treatment of
CC facial wrinkles and asymmetry and pathological neuronal
CC exocytosis-mediated pathological disorders and alterations manifested
CC e.g. by spasms and neurological and neurodegenerative disorders.
XX
SQ Sequence 19 AA;

Query Match 100.0%; Score 39; DB 22; Length 19;
Best Local Similarity 100.0%; Pred. No. 0.11;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 EANQRATK 8
          ||||||||
Db     10 EANQRATK 17
```

RESULT 13
AAW30100
ID AAW30100 standard; peptide; 20 AA.
XX
AC AAW30100;
XX
DT 06-APR-1998 (first entry)
XX
DE Neurotransmitter secretion inhibitor #4.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;

KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle
PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Claim 14; Page 32; 61pp; English.
XX
CC This sequence corresponds to residues 187-206 of the human 25 kD
CC synaptosomal associated protein (SNAP-25), and is a inhibitory agent of
CC the invention. The agents of the invention inhibit secretion of
CC neurotransmitter from neuronal cells and is an excitation-secretory
CC uncoupling peptide (I) of at least 20 amino acids (aa) all of which
CC correspond substantially to any one of AAW30097-W30102, or more
CC generally any (I) that inhibits 50% of catecholamine secretion from
CC bovine chromaffin cells at a concentration of 10 microM, especially 0.25
CC microM, or less. (I) are used, as a replacement for Clostridium toxin, to
CC inhibit release of neurotransmitters from synaptic vesicles, specifically
CC for reducing muscle spasticity. Also (I) may be labelled to allow in
CC vivo imaging of intracellular distribution of (I). Compounds for
CC delivering the drug to neural cells provide targeted drug delivery, e.g.
CC of substance P to brain tumours for induction of apoptosis. Unlike the
CC neurotoxins, (I) are not toxic or immunogenic and are more readily
CC available. Their therapeutic effect lasts for several days or weeks, so
CC lower doses or less frequent treatments are required.
XX
SQ Sequence 20 AA;

Query Match 100.0%; Score 39; DB 18; Length 20;
Best Local Similarity 100.0%; Pred. No. 0.12;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EANQRATK 8
||||||||
Db 8 EANQRATK 15

RESULT 14
AAW30099
ID AAW30099 standard; peptide; 26 AA.
XX
AC AAW30099;
XX
DT 06-APR-1998 (first entry)
XX
DE Neurotransmitter secretion inhibitor #3.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle
PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Claim 13; Page 31; 61pp; English.
XX
CC This sequence corresponds to residues 181-206 of the human 25 kD
CC synaptosomal associated protein (SNAP-25), and is a inhibitory agent of
CC the invention. The agents of the invention inhibit secretion of
CC neurotransmitter from neuronal cells and is an excitation-secretory
CC uncoupling peptide (I) of at least 20 amino acids (aa) all of which
CC correspond substantially to any one of AAW30097-W30102, or more
CC generally any (I) that inhibits 50% of catecholamine secretion from
CC bovine chromaffin cells at a concentration of 10 microM, especially 0.25
CC microM, or less. (I) are used, as a replacement for Clostridium toxin, to
CC inhibit release of neurotransmitters from synaptic vesicles, specifically
CC for reducing muscle spasticity. Also (I) may be labelled to allow in
CC vivo imaging of intracellular distribution of (I). Compounds for
CC delivering the drug to neural cells provide targeted drug delivery, e.g.
CC of substance P to brain tumours for induction of apoptosis. Unlike the
CC neurotoxins, (I) are not toxic or immunogenic and are more readily
CC available. Their therapeutic effect lasts for several days or weeks, so
CC lower doses or less frequent treatments are required.
XX
SQ Sequence 26 AA;

Query Match 100.0%; Score 39; DB 18; Length 26;
Best Local Similarity 100.0%; Pred. No. 0.16;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 EANQRATK 8
||||||||
Db 14 EANQRATK 21

RESULT 15
AAW30097
ID AAW30097 standard; peptide; 37 AA.
XX
AC AAW30097;
XX
DT 06-APR-1998 (first entry)
XX
DE Neurotransmitter secretion inhibitor #1.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX

PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle
PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Claim 1; Page 30; 61pp; English.
XX
CC This sequence corresponds to residues 170-206 of the human 25 kD
CC synaptosomal associated protein (SNAP-25), and is a inhibitory agent of
CC the invention. The agents of the invention inhibit secretion of
CC neurotransmitter from neuronal cells and is an excitation-secretory
CC uncoupling peptide (I) of at least 20 amino acids (aa) all of which
CC correspond substantially to any one of AAW30097-W30102, or more
CC generally any (I) that inhibits 50% of catecholamine secretion from
CC bovine chromaffin cells at a concentration of 10 microM, especially 0.25
CC microM, or less. (I) are used, as a replacement for Clostridium toxin, to
CC inhibit release of neurotransmitters from synaptic vesicles, specifically
CC for reducing muscle spasticity. Also (I) may be labelled to allow in
CC vivo imaging of intracellular distribution of (I). Compounds for
CC delivering the drug to neural cells provide targeted drug delivery, e.g.
CC of substance P to brain tumours for induction of apoptosis. Unlike the
CC neurotoxins, (I) are not toxic or immunogenic and are more readily
CC available. Their therapeutic effect lasts for several days or weeks, so
CC lower doses or less frequent treatments are required.
XX
SQ Sequence 37 AA;

Query Match 100.0%; Score 39; DB 18; Length 37;
Best Local Similarity 100.0%; Pred. No. 0.23;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy       1 EANQRATK 8
           ||||||||
Db      25 EANQRATK 32
```

Search completed: November 19, 2002, 17:34:25
Job time : 4.35135 secs

GenCore version 5.1.3

OM protein - protein search, using sw model

Run on: November 19, 2002, 17:32:44 ; Search time 86.2973 Seconds
(without alignments)
318.082 Million cell updates/sec

Title: PCT-US02-27145-2
Perfect score: 1048
Sequence: 1 MAEDADMRNELEEMQRRADQ.....SNKTRIDEANQRATKMLGSG 206

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_101002:*
1: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1980.DAT:*
2: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1981.DAT:*
3: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1982.DAT:*
4: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1983.DAT:*
5: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1984.DAT:*
6: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1985.DAT:*
7: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1986.DAT:*
8: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1987.DAT:*
9: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:*
10: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1989.DAT:*
11: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1990.DAT:*
12: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1991.DAT:*
13: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1992.DAT:*
14: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:*
15: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1994.DAT:*
16: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1995.DAT:*
17: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1996.DAT:*
18: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:*
19: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1998.DAT:*
20: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1999.DAT:*
21: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:*
22: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:*
23: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	1048	100.0	206	18	AAW30103	Synaptosomal assoc
2	1048	100.0	206	19	AAW79198	Mouse SNAP-25 poly
3	1048	100.0	206	19	AAW43426	Mouse synaptosomal
4	1048	100.0	206	22	AAU00246	Synaptosomal-assoc
5	1048	100.0	206	22	AAU00253	SNARE homologue, s
6	1043	99.5	206	22	AAU02640	Synaptosomal-assoc
7	1042	99.4	206	22	AAU00259	Synaptosomal-assoc
8	1042	99.4	206	22	AAU00260	Synaptosomal-assoc
9	1042	99.4	206	22	AAU00261	Synaptosomal-assoc
10	1042	99.4	206	22	AAU02638	Synaptosomal-assoc
11	1041	99.3	206	22	AAU00262	Synaptosomal-assoc
12	1039	99.1	206	22	AAU00257	Synaptosomal-assoc
13	1039	99.1	206	22	AAU00266	Synaptosomal-assoc
14	1037	99.0	206	22	AAU02171	Synaptosomal-assoc
15	1036	98.9	206	22	AAU00256	Synaptosomal-assoc
16	1036	98.9	206	22	AAU02639	Synaptosomal-assoc
17	1033	98.6	206	22	AAU00258	Synaptosomal-assoc
18	1026	97.9	203	22	AAU02636	Synaptosomal-assoc
19	1022	97.5	202	22	AAU00265	Synaptosomal-assoc
20	1017	97.0	201	22	AAU02637	Synaptosomal-assoc
21	1012	96.6	200	22	AAU00264	Synaptosomal-assoc
22	1009	96.3	198	22	AAU00255	Synaptosomal-assoc
23	1007	96.1	199	22	AAU00263	Synaptosomal-assoc
24	1004	95.8	206	22	AAU00252	SNARE homologue, s
25	625.5	59.7	212	22	ABB64447	Drosophila melanog
26	613.5	58.5	211	22	ABG02947	Novel human diagno
27	613.5	58.5	211	22	AAU00251	SNARE homologue, s
28	609.5	58.2	213	21	AAB57140	Human prostate can
29	587	56.0	116	23	AAO15165	Clostridial neurot
30	581	55.4	116	23	AAO15166	Clostridial neurot
31	451	43.0	106	21	AAG03825	Human secreted pro
32	451	43.0	106	21	AAG03826	Human secreted pro
33	403	38.5	86	22	AAB15584	Human SNAP-25 N-te
34	391.5	37.4	82	22	AAB15581	Human SNAP-25 N-te
35	361.5	34.5	129	21	AAB53705	Human colon cancer
36	353	33.7	70	17	AAR86823	SNAP-25 residues 1
37	310	29.6	64	21	AAG00764	Human secreted pro
38	253	24.1	513	21	AAG32996	Arabidopsis thalia
39	253	24.1	546	21	AAG32995	Arabidopsis thalia
40	253	24.1	714	21	AAG32994	Arabidopsis thalia
41	244	23.3	49	22	AAM57386	Human brain expres
42	230	21.9	247	21	AAG09027	Arabidopsis thalia
43	230	21.9	247	21	AAG23785	Arabidopsis thalia
44	230	21.9	247	21	AAG39336	Arabidopsis thalia
45	230	21.9	270	21	AAG23784	Arabidopsis thalia

ALIGNMENTS

RESULT 1
AAW30103
ID AAW30103 standard; peptide; 206 AA.
XX
AC AAW30103;
XX
DT 06-APR-1998 (first entry)
XX
DE Synaptosomal associated protein.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle

```
PT   spasticity, and for delivering drugs specifically to neural cells
XX
PS   Disclosure; Page 27-28; 61pp; English.
XX
CC   This sequence represents the human 25 kD synaptosomal associated protein
CC   (SNAP-25), which is an inhibitory agent of the invention. The agents of
CC   the invention inhibit secretion of neurotransmitter from neuronal cells
CC   and is an excitation-secretory uncoupling peptide (I) of at least 20
CC   amino acids (aa) all of which correspond substantially to any one of
CC   AAW30097-W30102, or more generally any (I) that inhibits 50% of
CC   catecholamine secretion from bovine chromaffin cells at a concentration
CC   of 10 microM, especially 0.25 microM, or less. (I) are used, as a
CC   replacement for Clostridium toxin, to inhibit release of
CC   neurotransmitters from synaptic vesicles, specifically for reducing
CC   muscle spasticity. Also (I) may be labelled to allow in vivo imaging of
CC   intracellular distribution of (I). Compounds for delivering the drug to
CC   neural cells provide targeted drug delivery, e.g. of substance P to
CC   brain tumours for induction of apoptosis. Unlike the neurotoxins, (I) are
CC   not toxic or immunogenic and are more readily available. Their
CC   therapeutic effect lasts for several days or weeks, so lower doses or
CC   less frequent treatments are required.
XX
SQ   Sequence   206 AA;

  Query Match             100.0%;  Score 1048;  DB 18;  Length 206;
  Best Local Similarity   100.0%;  Pred. No. 6.7e-91;
  Matches  206;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           |||||||||||||||||||||||||
Db     181 IMEKADSNKTRIDEANQRATKMLGSG 206


RESULT 2
AAW79198
ID   AAW79198 standard; Protein; 206 AA.
XX
AC   AAW79198;
XX
DT   25-NOV-1998  (first entry)
XX
DE   Mouse SNAP-25 polypeptide.
XX
KW   Hrs-2 polypeptide; ATP-preferring nucleotidase; SNAP-25; vesicle docking;
KW   calcium-regulated secretion; secretory vesicle; secretory process; brain;
KW   neurotransmitter release; presynaptic membrane; CNS disorder; depression;
KW   Parkinson's disease; endocrine system; hormonal imbalance; cell division;
KW   thought disorder; schizophrenia; degenerative disorder; anaesthesia; rat;
KW   immune system; antigen processing; immunomodulator; viral processing;
KW   central nervous system; vesicular release; affective disorder; human;
KW   anti-tumour application; membrane trafficking regulation; mouse.
XX
OS   Mus sp.
XX
PN   WO9838210-A2.
XX
PD   03-SEP-1998.
XX
PF   26-FEB-1998;   98WO-US03789.
XX
PR   26-FEB-1997;   97US-0039159.
XX
PA   (STRD ) UNIV LELAND STANFORD JUNIOR.
XX
PI   Bean AJ,  Scheller RH;
XX
DR   WPI; 1998-481140/41.
DR   N-PSDB; AAV57558.
XX
PT   New isolated Hrs-2 nucleotidase - used in assays to identify
PT   compounds capable of modulating calcium-regulatory secretion of
PT   secretory vesicles, such as in neurotransmitter release
XX
PS   Claim 16; Pages 42-44; 55pp; English.
XX
CC   This represents a mouse SNAP-25 polypeptide, a component of the protein
CC   polypeptides thought to underlie vesicle docking and fusion. The
CC   invention provides rat and human Hrs-2 polypeptides which are ATP-
CC   preferring nucleotidase that associate with SNAP-25. For identifying a
CC   compound capable of modulating calcium-regulated secretion of secretory
CC   vesicles, a SNAP-25 polypeptide can be contacted with a Hrs-2
CC   polypeptide, in the presence and absence of a test compound. The effect
CC   of the test compound on the extent of binding between the SNAP-25 and
CC   Hrs-2 polypeptides are measured and a compound is identified as effective
CC   if its measured effect on the extent of binding is above a threshold
CC   level. The products can be used for identifying drugs capable of
CC   affecting secretory processes, such as neurotransmitter release at the
CC   active zones of presynaptic membranes. Such drugs can be used for
CC   treating disorders or conditions of the central nervous system by
CC   selectively enhancing or inhibiting vesicular release in specific areas
CC   of the brain, including affective disorders (e.g. depression), disorders
CC   of thought (e.g. schizophrenia) and degenerative disorders ( Parkinson's
CC   disease), as well as applications such as anaesthesia.  The drugs can
CC   also be used therapeutically in other systems such as the endocrine
CC   system for treatment of hormonal imbalances, the immune system for
CC   intervention in antigen processing, secreted immunomodulators, and viral
CC   processing, as well as anti-tumour applications, such as regulation of
CC   membrane trafficking during rapid cell division.
XX
SQ   Sequence   206 AA;

  Query Match             100.0%;  Score 1048;  DB 19;  Length 206;
  Best Local Similarity   100.0%;  Pred. No. 6.7e-91;
  Matches  206;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           |||||||||||||||||||||||||
Db     181 IMEKADSNKTRIDEANQRATKMLGSG 206


RESULT 3
AAW43426
ID   AAW43426 standard; Protein; 206 AA.
XX
AC   AAW43426;
XX
DT   27-APR-1998  (first entry)
XX
DE   Mouse synaptosomal-associated protein-25.
XX
KW   Binding domain; mouse; syntaxin; synaptosomal-associated protein; CNS;
KW   neurotransmitter; presynaptic membrane; central nervous system; tumour;
```

KW neurodegenerative disease; hormonal disorder; immunological disorder.
XX
OS Mus sp.
XX
PN US5693476-A.
XX
PD 02-DEC-1997.
XX
PF 24-FEB-1995; 95US-0393985.
XX
PR 24-FEB-1995; 95US-0393985.
XX
PA (STRD) UNIV LELAND STANFORD JUNIOR.
XX
PI Scheller RH;
XX
DR WPI; 1998-031743/03.
DR N-PSDB; AAV01554.
XX
PT Screening assay for modulators of syntaxin binding - using peptide
PT comprising binding site of syntaxin, for identifying drugs useful
PT for treating CNS disorders, neuro-degenerative diseases, etc
XX
PS Disclosure; Column 67-72; 57pp; English.
XX
CC This amino acid sequence represents the mouse synaptosomal-associated
CC protein of 25 kD (SNAP-25). The invention relates to a method for
CC identifying a compound capable of affecting the binding of a
CC syntaxin-binding protein (SBP), e.g. SNAP-25, alpha-SNAP, n-secl or VAMP,
CC to syntaxin. The method comprises measuring the effect of the test
CC compound on the extent of binding between the SBP and the SBP-binding
CC site on syntaxin. The method can be used for identifying drugs capable
CC of inhibiting or stimulating neurotransmitter release at the active zones
CC of presynaptic membranes, which may be useful for treating CNS disorders,
CC affective or psychotic disorders, neurodegenerative diseases, hormonal or
CC immunological disorders or tumours.
XX
SQ Sequence 206 AA;

Query Match 100.0%; Score 1048; DB 19; Length 206;
Best Local Similarity 100.0%; Pred. No. 6.7e-91;
Matches 206; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy    181 IMEKADSNKTRIDEANQRATKMLGSG 206
          |||||||||||||||||||||||||
Db    181 IMEKADSNKTRIDEANQRATKMLGSG 206
```

RESULT 4
AAU00246
ID AAU00246 standard; Protein; 206 AA.
XX
AC AAU00246;
XX
DT 12-SEP-2001 (first entry)
XX
DE Synaptosomal-associated protein, SNAP25.
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; mutagenic; PCR primer; mouse;
KW N-ethylmaleimide-sensitive fusion protein;
KW soluble NSF-attachment protein receptor.
XX
OS Mus sp.
XX
XX
FH Key Location/Qualifiers
FT Cleavage-site 180..181
FT /note= "Peptide bond susceptible to cleavage by
FT clostridial neurotoxin"
FT Cleavage-site 197..198
FT /note= "Peptide bonds susceptible to cleavage by
FT clostridial neurotoxin"
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Disclosure; Fig 8; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25. The sequence was used to
CC create SNAP-25 double/single point mutants and C-terminal deletion
CC mutants used in a new method of treating a patient suffering from
CC poisoning or at risk of poisoning by a clostridial toxin, comprising
CC supplying a SNARE (soluble (N-ethylmaleimide-sensitive fusion protein)-
CC attachment protein receptor) to a cell of the patient, where the SNARE is
CC resistant to proteolysis by the toxin (toxin-resistant SNARE) and/or is
CC capable of inhibiting the toxin (toxin-inhibitory SNARE). The protein can
CC be used in a method of treating a patient in need of inhibition of SNARE-
CC dependent exocytosis from a cell capable of performing SNARE-dependent
CC exocytosis, comprises supplying a fragment, variant, fusion or derivative
CC of a SNARE or an inhibitory SNARE to the cell of the patient. The toxin
CC resistant or toxin inhibitory SNARE or a recombinant polynucleotide
CC encoding the SNARE is useful in the manufacture of a medicament for the
CC treatment of a patient suffering from poisoning or at risk of poisoning
CC by clostridial toxin, e.g. from botulism or tetanus. The fragment,
CC variant, fusion or derivative of a SNARE or of an inhibitory SNARE, or a
CC recombinant polynucleotide encoding either of these SNARE polypeptides
CC are useful in the manufacture of medicament for the treatment of a
CC patient in need of inhibition of SNARE-dependent exocytosis from a cell
CC capable of performing SNARE-dependent exocytosis. The method of treatment
CC is relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
XX
SQ Sequence 206 AA;

Query Match 100.0%; Score 1048; DB 22; Length 206;
Best Local Similarity 100.0%; Pred. No. 6.7e-91;
Matches 206; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
```

```
Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           ||||||||||||||||||||||||||
Db     181 IMEKADSNKTRIDEANQRATKMLGSG 206
```

RESULT 5
AAU00253
ID AAU00253 standard; Protein; 206 AA.
XX
AC AAU00253;
XX
DT 12-SEP-2001 (first entry)
XX
DE SNARE homologue, synaptosomal-associated protein, hSNAP25b.
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; hSNAP25b; human.
XX
OS Homo sapiens.
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
DR N-PSDB; AAS00370.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Disclosure; Fig 8; 130pp; English.
XX
CC The sequence represents the amino acid sequence of SNARE homologue,
CC synaptosomal-associated membrane protein, hSNAP25b, used during analysis
CC of SNAP-25. SNAP-25 mutants were used in a new method of treating a
CC patient suffering from poisoning or at risk of poisoning by a clostridial
CC toxin, comprising supplying a SNARE (soluble (N-ethylmaleimide-sensitive
CC fusion protein)-attachment protein receptor) to a cell of the patient,
CC where the SNARE is resistant to proteolysis by the toxin (toxin-resistant
CC SNARE) and/or is capable of inhibiting the toxin (toxin-inhibitory
CC SNARE). The protein can be used in a method of treating a patient in need
CC of inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis, comprises supplying a fragment,
CC variant, fusion or derivative of a SNARE or an inhibitory SNARE to the
CC cell of the patient. The toxin resistant or toxin inhibitory SNARE or a
CC recombinant polynucleotide encoding the SNARE is useful in the
CC manufacture of a medicament for the treatment of a patient suffering from
CC poisoning or at risk of poisoning by clostridial toxin, e.g. from
CC botulism or tetanus. The fragment, variant, fusion or derivative of a
CC SNARE or of an inhibitory SNARE, or a recombinant polynucleotide encoding
CC either of these SNARE polypeptides are useful in the manufacture of
CC medicament for the treatment of a patient in need of inhibition of SNARE-
CC dependent exocytosis from a cell capable of performing SNARE-dependent
CC exocytosis. The method of treatment is relatively fast, thus
CC alleviating the symptoms when most severe and taking the patient out of
CC critical state.
XX
SQ Sequence 206 AA;

```
  Query Match           100.0%;  Score 1048;  DB 22;  Length 206;
  Best Local Similarity 100.0%;  Pred. No. 6.7e-91;
  Matches  206;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           ||||||||||||||||||||||||||
Db     181 IMEKADSNKTRIDEANQRATKMLGSG 206
```

RESULT 6
AAU02640
ID AAU02640 standard; Protein; 206 AA.
XX
AC AAU02640;
XX
DT 12-SEP-2001 (first entry)
XX
DE Synaptosomal-associated protein, SNAP25, mutant L203A.
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; mouse; mutant; mutein;
KW N-ethylmaleimide-sensitive fusion protein;
KW soluble NSF-attachment protein receptor.
XX
OS Mus sp.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 203
FT /note= "Wild-type Leu substituted by Ala"
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Example 1; Page - ; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25, mutant L203A, used in a new
CC method of treating a patient suffering from poisoning or at risk of
CC poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC to a cell of the patient, where the SNARE is resistant to proteolysis by
CC the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC treating a patient in need of inhibition of SNARE-dependent exocytosis

```
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   206 AA;

  Query Match           99.5%;  Score 1043;  DB 22;  Length 206;
  Best Local Similarity   99.5%;  Pred. No. 2e-90;
  Matches  205;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           |||||||||||||||||||| |||
Db     181 IMEKADSNKTRIDEANQRATKMAGSG 206


RESULT 7
AAU00259
ID   AAU00259 standard; Protein; 206 AA.
XX
AC   AAU00259;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant R198T.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant R198T used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   206 AA;

  Query Match           99.4%;  Score 1042;  DB 22;  Length 206;
  Best Local Similarity   99.5%;  Pred. No. 2.5e-90;
  Matches  205;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           |||||||||||||||||| ||||||||
Db     181 IMEKADSNKTRIDEANQTATKMLGSG 206


RESULT 8
AAU00260
ID   AAU00260 standard; Protein; 206 AA.
XX
AC   AAU00260;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant Q197A
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
```

```
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 197
FT                   /note= "Wild-type Gln substituted by Ala"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant Q197A, used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   206 AA;

  Query Match             99.4%;  Score 1042;  DB 22;  Length 206;
  Best Local Similarity   99.5%;  Pred. No. 2.5e-90;
  Matches  205;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           |||||||||||||||| |||||||||
Db     181 IMEKADSNKTRIDEANARATKMLGSG 206


RESULT 9
AAU00261
ID   AAU00261 standard; Protein; 206 AA.
XX
AC   AAU00261;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant R198A.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Ala"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant R198A used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
```

```
XX
SQ   Sequence   206 AA;

  Query Match           99.4%;  Score 1042;  DB 22;  Length 206;
  Best Local Similarity   99.5%;  Pred. No. 2.5e-90;
  Matches  205;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy    181 IMEKADSNKTRIDEANQRATKMLGSG 206
          |||||||||||||||| ||||||||
Db    181 IMEKADSNKTRIDEANQAATKMLGSG 206


RESULT 10
AAU02638
ID   AAU02638 standard; Protein; 206 AA.
XX
AC   AAU02638;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant M202A.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 202
FT                   /note= "Wild-type Met substituted by Ala"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant M202A, used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   206 AA;

  Query Match           99.4%;  Score 1042;  DB 22;  Length 206;
  Best Local Similarity   99.5%;  Pred. No. 2.5e-90;
  Matches  205;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy    181 IMEKADSNKTRIDEANQRATKMLGSG 206
          |||||||||||||||||||| ||||
Db    181 IMEKADSNKTRIDEANQRATKALGSG 206


RESULT 11
AAU00262
ID   AAU00262 standard; Protein; 206 AA.
XX
AC   AAU00262;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant Q197K,R198K.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 197
FT                   /note= "Wild-type Gln substituted by Lys"
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Lys"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
```

XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Example 1; Page - ; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25, mutant Q197K/R198K, used in a new
CC method of treating a patient suffering from poisoning or at risk of
CC poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC to a cell of the patient, where the SNARE is resistant to proteolysis by
CC the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC treating a patient in need of inhibition of SNARE-dependent exocytosis
CC from a cell capable of performing SNARE-dependent exocytosis, comprises
CC supplying a fragment, variant, fusion or derivative of a SNARE or an
CC inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC useful in the manufacture of a medicament for the treatment of a patient
CC suffering from poisoning or at risk of poisoning by clostridial toxin,
CC e.g. from botulism or tetanus. The fragment, variant, fusion or
CC derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC polynucleotide encoding either of these SNARE polypeptides are useful in
CC the manufacture of medicament for the treatment of a patient in need of
CC inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis. The method of treatment is
CC relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
CC Note: The present sequence is not shown in the specification but is
CC derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ Sequence 206 AA;

Query Match 99.3%; Score 1041; DB 22; Length 206;
Best Local Similarity 99.0%; Pred. No. 3.1e-90;
Matches 204; Conservative 2; Mismatches 0; Indels 0; Gaps 0;

```
Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           ||||||||||||||::||||||||
Db     181 IMEKADSNKTRIDEANKKATKMLGSG 206
```

RESULT 12
AAU00257
ID AAU00257 standard; Protein; 206 AA.
XX
AC AAU00257;
XX
DT 12-SEP-2001 (first entry)
XX
DE Synaptosomal-associated protein, SNAP25, mutant Q197A/R198K.
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; mouse; mutant; mutein;
KW N-ethylmaleimide-sensitive fusion protein;
KW soluble NSF-attachment protein receptor.
XX
OS Mus sp.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 197
FT /note= "Wild-type Gln substituted by Ala"
FT Misc-difference 198
FT /note= "Wild-type Arg substituted by Lys"
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Example 1; Page - ; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25, mutant Q197A/R198K, used in a new
CC method of treating a patient suffering from poisoning or at risk of
CC poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC to a cell of the patient, where the SNARE is resistant to proteolysis by
CC the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC treating a patient in need of inhibition of SNARE-dependent exocytosis
CC from a cell capable of performing SNARE-dependent exocytosis, comprises
CC supplying a fragment, variant, fusion or derivative of a SNARE or an
CC inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC useful in the manufacture of a medicament for the treatment of a patient
CC suffering from poisoning or at risk of poisoning by clostridial toxin,
CC e.g. from botulism or tetanus. The fragment, variant, fusion or
CC derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC polynucleotide encoding either of these SNARE polypeptides are useful in
CC the manufacture of medicament for the treatment of a patient in need of
CC inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis. The method of treatment is
CC relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
CC Note: The present sequence is not shown in the specification but is
CC derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ Sequence 206 AA;

Query Match 99.1%; Score 1039; DB 22; Length 206;
Best Local Similarity 99.0%; Pred. No. 4.8e-90;
Matches 204; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```
Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
```

```
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy    181 IMEKADSNKTRIDEANQRATKMLGSG 206
          |||||||||||||||| :||||||||
Db    181 IMEKADSNKTRIDEANAKATKMLGSG 206


RESULT 13
AAU00266
ID   AAU00266 standard; Protein; 206 AA.
XX
AC   AAU00266;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant Q197K/R198H.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 197
FT                   /note= "Wild-type Gln substituted by Lys"
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by His"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant Q197K/R198H, used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   206 AA;

  Query Match            99.1%;  Score 1039;  DB 22;  Length 206;
  Best Local Similarity  99.0%;  Pred. No. 4.8e-90;
  Matches  204;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy    181 IMEKADSNKTRIDEANQRATKMLGSG 206
          |||||||||||||||| :|||||||
Db    181 IMEKADSNKTRIDEANKHATKMLGSG 206


RESULT 14
AAU02171
ID   AAU02171 standard; Protein; 206 AA.
XX
AC   AAU02171;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant R198T/L203A.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
FT   Misc-difference 203
FT                   /note= "Wild-type Leu substituted by Ala"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
```

```
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant R198T/L203A, used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   206 AA;

  Query Match             99.0%;  Score 1037;  DB 22;  Length 206;
  Best Local Similarity   99.0%;  Pred. No. 7.3e-90;
  Matches  204;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           |||||||||||||||| |||| |||
Db     181 IMEKADSNKTRIDEANQTATKMAGSG 206


RESULT 15
AAU00256
ID   AAU00256 standard; Protein; 206 AA.
XX
AC   AAU00256;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant Q197A/R198A.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 197
FT                   /note= "Wild-type Gln substituted by Ala"
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Ala"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant Q197A/R198A, used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   206 AA;

  Query Match             98.9%;  Score 1036;  DB 22;  Length 206;
  Best Local Similarity   99.0%;  Pred. No. 9.1e-90;
  Matches  204;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAEDADMRNELEEMQRRADQLADESLESTRRMLQLVEESKDAGIRTLVMLDEQGEQLERI 60

Qy      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 EEGMDQINKDMKEAEKNLTDLGKFCGLCVCPCNKLKSSDAYKKAWGNNQDGVVASQPARV 120

Qy     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 VDEREQMAISGGFIRRVTNDARENEMDENLEQVSGIIGNLRHMALDMGNEIDTQNRQIDR 180

Qy     181 IMEKADSNKTRIDEANQRATKMLGSG 206
           |||||||||||||||| ||||||||
Db     181 IMEKADSNKTRIDEANAAATKMLGSG 206
```

Search completed: November 19, 2002, 17:34:26
Job time : 87.2973 secs

GenCore version 5.1.3
Copyright (c) 1993 - 2002 Compugen Ltd.

OM protein - protein search, using sw model

Run on: November 19, 2002, 17:32:44 ; Search time 3.35135 Seconds
(without alignments)
318.082 Million cell updates/sec

Title: PCT-US02-27145-8
Perfect score: 39
Sequence: 1 QIDRIMEK 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_101002:*
1: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1980.DAT:*
2: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1981.DAT:*
3: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1982.DAT:*
4: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1983.DAT:*
5: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1984.DAT:*
6: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1985.DAT:*
7: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1986.DAT:*
8: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1987.DAT:*
9: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:*
10: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1989.DAT:*
11: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1990.DAT:*
12: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1991.DAT:*
13: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1992.DAT:*
14: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:*
15: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1994.DAT:*
16: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1995.DAT:*
17: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1996.DAT:*
18: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:*
19: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1998.DAT:*
20: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1999.DAT:*
21: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:*
22: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:*
23: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	39	100.0	20	18	AAW30098	Neurotransmitter s
2	39	100.0	37	18	AAW30097	Neurotransmitter s
3	39	100.0	49	22	AAM57386	Human brain expres
4	39	100.0	70	17	AAR86823	SNAP-25 residues 1
5	39	100.0	86	22	AAB15584	Human SNAP-25 N-te
6	39	100.0	116	23	AAO15165	Clostridial neurot
7	39	100.0	116	23	AAO15166	Clostridial neurot
8	39	100.0	198	22	AAU00255	Synaptosomal-assoc
9	39	100.0	199	22	AAU00263	Synaptosomal-assoc
10	39	100.0	200	22	AAU00264	Synaptosomal-assoc
11	39	100.0	201	22	AAU02637	Synaptosomal-assoc
12	39	100.0	202	22	AAU00265	Synaptosomal-assoc
13	39	100.0	203	22	AAU02636	Synaptosomal-assoc
14	39	100.0	206	18	AAW30103	Synaptosomal assoc
15	39	100.0	206	19	AAW79198	Mouse SNAP-25 poly
16	39	100.0	206	19	AAW43426	Mouse synaptosomal
17	39	100.0	206	22	AAU00246	Synaptosomal-assoc
18	39	100.0	206	22	AAU00252	SNARE homologue, s
19	39	100.0	206	22	AAU00253	SNARE homologue, s
20	39	100.0	206	22	AAU00256	Synaptosomal-assoc
21	39	100.0	206	22	AAU00257	Synaptosomal-assoc
22	39	100.0	206	22	AAU00258	Synaptosomal-assoc
23	39	100.0	206	22	AAU00259	Synaptosomal-assoc
24	39	100.0	206	22	AAU00260	Synaptosomal-assoc
25	39	100.0	206	22	AAU00261	Synaptosomal-assoc
26	39	100.0	206	22	AAU00262	Synaptosomal-assoc
27	39	100.0	206	22	AAU00266	Synaptosomal-assoc
28	39	100.0	206	22	AAU02171	Synaptosomal-assoc
29	39	100.0	206	22	AAU02638	Synaptosomal-assoc
30	39	100.0	206	22	AAU02639	Synaptosomal-assoc
31	39	100.0	206	22	AAU02640	Synaptosomal-assoc
32	34	87.2	200	22	AAG82046	S. epidermidis ope
33	34	87.2	200	22	AAG82648	S. epidermidis ope
34	34	87.2	208	23	ABP38940	Staphylococcus epi
35	33	84.6	841	22	ABG09845	Novel human diagno
36	33	84.6	1643	22	ABB63371	Drosophila melanog
37	33	84.6	1825	22	ABG09849	Novel human diagno
38	33	84.6	1909	22	ABG21157	Novel human diagno
39	32	82.1	35	23	AAU78070	Influenza strain A
40	32	82.1	566	21	AAB29746	Influenza virus ha
41	31	79.5	59	22	AAO02582	Human polypeptide
42	31	79.5	135	20	AAY36760	Amino acid sequenc
43	31	79.5	349	22	ABG01597	Novel human diagno
44	31	79.5	429	21	AAG14050	Arabidopsis thalia
45	31	79.5	429	21	AAG51986	Arabidopsis thalia

ALIGNMENTS

RESULT 1
AAW30098
ID AAW30098 standard; peptide; 20 AA.
XX
AC AAW30098;
XX
DT 06-APR-1998 (first entry)
XX
DE Neurotransmitter secretion inhibitor #2.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neurotransmitter release - used particularly for treating muscle

PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Claim 12; Page 31; 61pp; English.
XX
CC This sequence corresponds to residues 170-189 of the human 25 kD
CC synaptosomal associated protein (SNAP-25), and is a inhibitory agent of
CC the invention. The agents of the invention inhibit secretion of
CC neurotransmitter from neuronal cells and is an excitation-secretory
CC uncoupling peptide (I) of at least 20 amino acids (aa) all of which
CC correspond substantially to any one of AAW30097-W30102, or more
CC generally any (I) that inhibits 50% of catecholamine secretion from
CC bovine chromaffin cells at a concentration of 10 microM, especially 0.25
CC microM, or less. (I) are used, as a replacement for Clostridium toxin, to
CC inhibit release of neurotransmitters from synaptic vesicles, specifically
CC for reducing muscle spasticity. Also (I) may be labelled to allow in
CC vivo imaging of intracellular distribution of (I). Compounds for
CC delivering the drug to neural cells provide targeted drug delivery, e.g.
CC of substance P to brain tumours for induction of apoptosis. Unlike the
CC neurotoxins, (I) are not toxic or immunogenic and are more readily
CC available. Their therapeutic effect lasts for several days or weeks, so
CC lower doses or less frequent treatments are required.
XX
SQ Sequence 20 AA;

Query Match 100.0%; Score 39; DB 18; Length 20;
Best Local Similarity 100.0%; Pred. No. 0.4;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 QIDRIMEK 8
||||||||
Db 8 QIDRIMEK 15

RESULT 2
AAW30097
ID AAW30097 standard; peptide; 37 AA.
XX
AC AAW30097;
XX
DT 06-APR-1998 (first entry)
XX
DE Neurotransmitter secretion inhibitor #1.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle
PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Claim 1; Page 30; 61pp; English.
XX
CC This sequence corresponds to residues 170-206 of the human 25 kD
CC synaptosomal associated protein (SNAP-25), and is a inhibitory agent of
CC the invention. The agents of the invention inhibit secretion of
CC neurotransmitter from neuronal cells and is an excitation-secretory
CC uncoupling peptide (I) of at least 20 amino acids (aa) all of which
CC correspond substantially to any one of AAW30097-W30102, or more
CC generally any (I) that inhibits 50% of catecholamine secretion from
CC bovine chromaffin cells at a concentration of 10 microM, especially 0.25
CC microM, or less. (I) are used, as a replacement for Clostridium toxin, to
CC inhibit release of neurotransmitters from synaptic vesicles, specifically
CC for reducing muscle spasticity. Also (I) may be labelled to allow in
CC vivo imaging of intracellular distribution of (I). Compounds for
CC delivering the drug to neural cells provide targeted drug delivery, e.g.
CC of substance P to brain tumours for induction of apoptosis. Unlike the
CC neurotoxins, (I) are not toxic or immunogenic and are more readily
CC available. Their therapeutic effect lasts for several days or weeks, so
CC lower doses or less frequent treatments are required.
XX
SQ Sequence 37 AA;

Query Match 100.0%; Score 39; DB 18; Length 37;
Best Local Similarity 100.0%; Pred. No. 0.73;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 QIDRIMEK 8
||||||||
Db 8 QIDRIMEK 15

RESULT 3
AAM57386
ID AAM57386 standard; Protein; 49 AA.
XX
AC AAM57386;
XX
DT 05-NOV-2001 (first entry)
XX
DE Human brain expressed single exon probe encoded protein SEQ ID NO: 29491.
XX
KW Human; brain expressed exon; gene expression analysis; probe;
KW microarray; Alzheimer's disease; multiple sclerosis; schizophrenia;
KW epilepsy; cancer.
XX
OS Homo sapiens.
XX
PN WO200157275-A2.
XX
PD 09-AUG-2001.
XX
PF 30-JAN-2001; 2001WO-US00667.
XX
PR 04-FEB-2000; 2000US-0180312.
PR 26-MAY-2000; 2000US-0207456.
PR 30-JUN-2000; 2000US-0608408.
PR 03-AUG-2000; 2000US-0632366.
PR 21-SEP-2000; 2000US-0234687.
PR 27-SEP-2000; 2000US-0236359.
PR 04-OCT-2000; 2000GB-0024263.
XX
PA (MOLE-) MOLECULAR DYNAMICS INC.
XX
PI Penn SG, Hanzel DK, Chen W, Rank DR;
XX
DR WPI; 2001-483446/52.
XX
PT Single exon nucleic acid probes for analyzing gene expression in human
PT brains -
XX
PS Example 4; SEQ ID NO: 29491; 650pp + Sequence Listing; English.
XX
CC The present invention provides a number of single exon nucleic acid
CC probes which are derived from genomic sequences expressed in the human
CC brain. They can be used to measure gene expression in brain cell samples,
CC which may enable the diagnosis and improved treatment of nervous system
CC diseases such as Alzheimer's disease, multiple sclerosis, schizophrenia,
CC epilepsy and cancers. The present sequence is a protein encoded by one of

```
CC   the probes of the invention.
XX
SQ   Sequence   49 AA;

  Query Match            100.0%;  Score 39;  DB 22;  Length 49;
  Best Local Similarity  100.0%;  Pred. No. 0.96;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 QIDRIMEK 8
          ||||||||
Db     41 QIDRIMEK 48


RESULT 4
AAR86823
ID   AAR86823 standard; Peptide; 70 AA.
XX
AC   AAR86823;
XX
DT   15-AUG-1996  (first entry)
XX
DE   SNAP-25 residues 137-206.
XX
KW   VAMP; vesicle-associated membrane protein; SNAP-25; syntaxin;
KW   neurotransmitter; neurotoxin; botulinum; botulism; cleavage;
KW   substrate; antibody; detection; assay.
XX
OS   Synthetic.
XX
PN   WO9533850-A1.
XX
PD   14-DEC-1995.
XX
PF   02-JUN-1995;   95WO-GB01279.
XX
PR   03-JUN-1994;   94GB-0011138.
XX
PA   (CAMR-) CAMR CENT APPLIED MICROBIOLOGY & RES.
PA   (MICR-) MICROBIOLOGICAL RES AUTHORITY.
XX
PI   Hallis B,  James BAF,  Quinn CP,  Shone CC;
XX
DR   WPI; 1996-040249/04.
XX
PT   Assay for botulinum or tetanus toxin - by combining test cpd. with
PT   substrate which is cleaved by the toxin, and antibody specific for
PT   the cleaved but not uncleaved substrate
XX
PS   Example 4; Page 19; 48pp; English.
XX
CC   The botulinum neurotoxins possess highly specific zinc-endopeptidase
CC   activities within their light sub-units. Depending on the neurotoxin
CC   type these act to cleave small proteins within the nerve cell which are
CC   involved in neurotransmitter release.  Antibodies are used in assays
CC   which detect cleaved but not uncleaved substrate. Assays for botulinum
CC   types A and E use the present sequence as a substrate. The sequence is
CC   SNAP-25 protein, residues 137-206.
XX
SQ   Sequence   70 AA;

  Query Match            100.0%;  Score 39;  DB 17;  Length 70;
  Best Local Similarity  100.0%;  Pred. No. 1.4;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 QIDRIMEK 8
          ||||||||
Db     41 QIDRIMEK 48


RESULT 5
AAB15584
ID   AAB15584 standard; peptide; 86 AA.
XX
AC   AAB15584;
XX
DT   02-MAR-2001  (first entry)
XX
DE   Human SNAP-25 N-terminal peptide #4.
XX
KW   Dermatological; neuroprotective; relaxant; neuronal exocytosis modulator;
KW   SNAP-25; synaptosomal-associated protein 25; facial wrinkle; asymmetry;
KW   neurodegenerative disorder.
XX
OS   Homo sapiens.
XX
PN   WO200064932-A1.
XX
PD   02-NOV-2000.
XX
PF   18-FEB-2000; 2000WO-ES00058.
XX
PR   23-APR-1999;   99ES-0000844.
XX
PA   (LIPO-) LIPOTEC SA.
XX
PI   Blanes Mira MC,  Llobregat Hernandez MM,  Gil Tebar AI;
PI   Fernandez Ballester GJ,  Planell Cases RM,  Ferrer Montiel AV;
PI   Viniegra Bover S,  Gutierrez Perez LM,  Carbonell Castell T;
PI   Perez Paya E;
XX
DR   WPI; 2001-007091/01.
XX
PT   New peptides containing amino acid sequences from known proteins for
PT   treatment of neurological disorders  -
XX
PS   Claim 16; Page 32-33; 40pp; Spanish.
XX
CC   The invention relates to new peptides comprising 3-30 contiguous amino
CC   acids from the N-terminus of the protein SNAP-25
CC   (synaptosomal-associated protein 25). The peptides AAB15581-B15586
CC   represent examples of the peptides of the invention. The peptides have
CC   neuronal exocytosis inhibitory activity and are used for treatment of
CC   facial wrinkles and asymmetry and pathological neuronal
CC   exocytosis-mediated pathological disorders and alterations manifested
CC   e.g. by spasms and neurological and neurodegenerative disorders.
XX
SQ   Sequence   86 AA;

  Query Match            100.0%;  Score 39;  DB 22;  Length 86;
  Best Local Similarity  100.0%;  Pred. No. 1.7;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 QIDRIMEK 8
          ||||||||
Db     57 QIDRIMEK 64


RESULT 6
AAO15165
ID   AAO15165 standard; peptide; 116 AA.
XX
AC   AAO15165;
XX
DT   02-SEP-2002  (first entry)
XX
DE   Clostridial neurotoxin protease substrate peptide 4.
XX
KW   Clostridial neurotoxin substrate; botulinum neurotoxin substrate; FRET;
KW   fluorescence resonant energy transfer assay; quenched-signal;
KW   clostridial neurotoxin detection; food.
XX
OS   Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "S-fluoresceinyl-cysteine"
```

```
FT   Cleavage-site   89..90
FT                   /note= "The peptide is cleaved between these two
FT                   residues by type E Clostridium botulinum neurotoxin"
FT   Cleavage-site   106..107
FT                   /note= "The peptide is cleaved between these two
FT                   residues by type A Clostridium botulinum neurotoxin"
XX
PN   WO200225284-A2.
XX
PD   28-MAR-2002.
XX
PF   25-SEP-2001; 2001WO-US30188.
XX
PR   25-SEP-2000; 2000US-235050P.
XX
PA   (USME-) US MEDICAL RES INST INFECTIOUS DISEASES.
XX
PI   Schmidt JJ,  Stafford RG;
XX
DR   WPI; 2002-499829/53.
XX
PT   Substrate useful in e.g. an assay for the protease activity of
PT   clostridial neurotoxin, comprises modified peptide or protein  -
XX
PS   Claim 22; Page 16; 48pp; English.
XX
CC   The invention comprises clostridial neurotoxin substrate peptides which
CC   can serve as fluorescence resonant energy transfer assay (FRET) or
CC   quenched-signal substrates in assays for the proteolytic activities of
CC   clostridial neurotoxins. The invention further comprises Clostridium
CC   botulinum neurotoxin substrate peptides that can serve as immobilised
CC   substrates (i.e. bound to a solid phase) in assays for the proteolytic
CC   activities of clostridial neurotoxins. The clostridial (including the
CC   Clostridium botulinum) neurotoxin substrate peptides are useful for
CC   detecting the presence of clostridial neurotoxins in a sample (e.g. food
CC   or an environmental sample). The present amino acid sequence represents a
CC   clostridial neurotoxin substrate peptide of the invention.
XX
SQ   Sequence   116 AA;

  Query Match             100.0%;  Score 39;  DB 23;  Length 116;
  Best Local Similarity   100.0%;  Pred. No. 2.2;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 QIDRIMEK 8
           ||||||||
Db      86 QIDRIMEK 93


RESULT 7
AAO15166
ID   AAO15166 standard; peptide; 116 AA.
XX
AC   AAO15166;
XX
DT   02-SEP-2002  (first entry)
XX
DE   Clostridial neurotoxin protease substrate peptide 5.
XX
KW   Clostridial neurotoxin substrate; botulinum neurotoxin substrate; FRET;
KW   fluorescence resonant energy transfer assay; quenched-signal;
KW   clostridial neurotoxin detection; food.
XX
OS   Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "S-fluoresceinyl-cysteine"
FT   Cleavage-site   89..90
FT                   /note= "The peptide is cleaved between these two
FT                   residues by type E Clostridium botulinum neurotoxin"
XX
PN   WO200225284-A2.
XX
PD   28-MAR-2002.
XX
PF   25-SEP-2001; 2001WO-US30188.
XX
PR   25-SEP-2000; 2000US-235050P.
XX
PA   (USME-) US MEDICAL RES INST INFECTIOUS DISEASES.
XX
PI   Schmidt JJ,  Stafford RG;
XX
DR   WPI; 2002-499829/53.
XX
PT   Substrate useful in e.g. an assay for the protease activity of
PT   clostridial neurotoxin, comprises modified peptide or protein  -
XX
PS   Claim 28; Page 17; 48pp; English.
XX
CC   The invention comprises clostridial neurotoxin substrate peptides which
CC   can serve as fluorescence resonant energy transfer assay (FRET) or
CC   quenched-signal substrates in assays for the proteolytic activities of
CC   clostridial neurotoxins. The invention further comprises Clostridium
CC   botulinum neurotoxin substrate peptides that can serve as immobilised
CC   substrates (i.e. bound to a solid phase) in assays for the proteolytic
CC   activities of clostridial neurotoxins. The clostridial (including the
CC   Clostridium botulinum) neurotoxin substrate peptides are useful for
CC   detecting the presence of clostridial neurotoxins in a sample (e.g. food
CC   or an environmental sample). The present amino acid sequence represents a
CC   clostridial neurotoxin substrate peptide of the invention.
XX
SQ   Sequence   116 AA;

  Query Match             100.0%;  Score 39;  DB 23;  Length 116;
  Best Local Similarity   100.0%;  Pred. No. 2.2;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 QIDRIMEK 8
           ||||||||
Db      86 QIDRIMEK 93


RESULT 8
AAU00255
ID   AAU00255 standard; Protein; 198 AA.
XX
AC   AAU00255;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, C-terminal deletion 1-198.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
```

```
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, C-terminal deletion 1-198, used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   198 AA;

  Query Match             100.0%;  Score 39;  DB 22;  Length 198;
  Best Local Similarity   100.0%;  Pred. No. 3.7;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 QIDRIMEK 8
           ||||||||
Db     177 QIDRIMEK 184


RESULT 9
AAU00263
ID   AAU00263 standard; Protein; 199 AA.
XX
AC   AAU00263;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant 1-199(R198T).
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant 1-199(R198T), used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   199 AA;

  Query Match             100.0%;  Score 39;  DB 22;  Length 199;
  Best Local Similarity   100.0%;  Pred. No. 3.8;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 QIDRIMEK 8
           ||||||||
Db     177 QIDRIMEK 184


RESULT 10
AAU00264
ID   AAU00264 standard; Protein; 200 AA.
XX
AC   AAU00264;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant 1-200(R198T).
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
```

XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Example 1; Page - ; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25, mutant 1-200(R198T), used in a new
CC method of treating a patient suffering from poisoning or at risk of
CC poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC to a cell of the patient, where the SNARE is resistant to proteolysis by
CC the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC treating a patient in need of inhibition of SNARE-dependent exocytosis
CC from a cell capable of performing SNARE-dependent exocytosis, comprises
CC supplying a fragment, variant, fusion or derivative of a SNARE or an
CC inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC useful in the manufacture of a medicament for the treatment of a patient
CC suffering from poisoning or at risk of poisoning by clostridial toxin,
CC e.g. from botulism or tetanus. The fragment, variant, fusion or
CC derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC polynucleotide encoding either of these SNARE polypeptides are useful in
CC the manufacture of medicament for the treatment of a patient in need of
CC inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis. The method of treatment is
CC relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
CC Note: The present sequence is not shown in the specification but is
CC derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ Sequence 200 AA;

Query Match 100.0%; Score 39; DB 22; Length 200;
Best Local Similarity 100.0%; Pred. No. 3.8;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 QIDRIMEK 8
||||||||
Db 177 QIDRIMEK 184

RESULT 11
AAU02637
ID AAU02637 standard; Protein; 201 AA.
XX
AC AAU02637;
XX
DT 12-SEP-2001 (first entry)
XX
DE Synaptosomal-associated protein, SNAP25, mutant 1-201(R198T).
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; mouse; mutant; mutein;
KW N-ethylmaleimide-sensitive fusion protein;
KW soluble NSF-attachment protein receptor.
XX
OS Mus sp.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 198
FT /note= "Wild-type Arg substituted by Thr"
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Example 1; Page - ; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25, mutant 1-201(R198T), used in a new
CC method of treating a patient suffering from poisoning or at risk of
CC poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC to a cell of the patient, where the SNARE is resistant to proteolysis by
CC the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC treating a patient in need of inhibition of SNARE-dependent exocytosis
CC from a cell capable of performing SNARE-dependent exocytosis, comprises
CC supplying a fragment, variant, fusion or derivative of a SNARE or an
CC inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC useful in the manufacture of a medicament for the treatment of a patient
CC suffering from poisoning or at risk of poisoning by clostridial toxin,
CC e.g. from botulism or tetanus. The fragment, variant, fusion or
CC derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC polynucleotide encoding either of these SNARE polypeptides are useful in
CC the manufacture of medicament for the treatment of a patient in need of
CC inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis. The method of treatment is
CC relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
CC Note: The present sequence is not shown in the specification but is
CC derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ Sequence 201 AA;

Query Match 100.0%; Score 39; DB 22; Length 201;
Best Local Similarity 100.0%; Pred. No. 3.8;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 QIDRIMEK 8
||||||||
Db 177 QIDRIMEK 184

RESULT 12
AAU00265
ID AAU00265 standard; Protein; 202 AA.
XX
AC AAU00265;
XX
DT 12-SEP-2001 (first entry)
XX

```
DE   Synaptosomal-associated protein, SNAP25, mutant 1-202(R198T).
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant 1-202(R198T), used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   202 AA;

  Query Match            100.0%;  Score 39;  DB 22;  Length 202;
  Best Local Similarity  100.0%;  Pred. No. 3.8;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 QIDRIMEK 8
           ||||||||
Db     177 QIDRIMEK 184


RESULT 13
AAU02636
ID   AAU02636 standard; Protein; 203 AA.
XX
AC   AAU02636;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant 1-203(R198T).
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant 1-203(R198T), used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   203 AA;

  Query Match            100.0%;  Score 39;  DB 22;  Length 203;
  Best Local Similarity  100.0%;  Pred. No. 3.8;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
```

```
Qy      1 QIDRIMEK 8
          ||||||||
Db    177 QIDRIMEK 184


RESULT 14
AAW30103
ID   AAW30103 standard; peptide; 206 AA.
XX
AC   AAW30103;
XX
DT   06-APR-1998  (first entry)
XX
DE   Synaptosomal associated protein.
XX
KW   Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW   excitation-secretory uncoupling peptide; catecholamine secretion;
KW   bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW   synaptosomal associated protein; SNAP-25.
XX
OS   Homo sapiens.
XX
PN   WO9734620-A1.
XX
PD   25-SEP-1997.
XX
PF   18-MAR-1997;   97WO-US04393.
XX
PR   18-MAR-1996;   96US-0013599.
XX
PA   (REGC ) UNIV CALIFORNIA.
XX
PI   Montal M;
XX
DR   WPI; 1997-479986/44.
XX
PT   Excitation-secretory uncoupling peptide(s) for inhibiting
PT   neuro:transmitter release - used particularly for treating muscle
PT   spasticity, and for delivering drugs specifically to neural cells
XX
PS   Disclosure; Page 27-28; 61pp; English.
XX
CC   This sequence represents the human 25 kD synaptosomal associated protein
CC   (SNAP-25), which is an inhibitory agent of the invention. The agents of
CC   the invention inhibit secretion of neurotransmitter from neuronal cells
CC   and is an excitation-secretory uncoupling peptide (I) of at least 20
CC   amino acids (aa) all of which correspond substantially to any one of
CC   AAW30097-W30102, or more generally any (I) that inhibits 50% of
CC   catecholamine secretion from bovine chromaffin cells at a concentration
CC   of 10 microM, especially 0.25 microM, or less. (I) are used, as a
CC   replacement for Clostridium toxin, to inhibit release of
CC   neurotransmitters from synaptic vesicles, specifically for reducing
CC   muscle spasticity. Also (I) may be labelled to allow in vivo imaging of
CC   intracellular distribution of (I). Compounds for delivering the drug to
CC   neural cells provide targeted drug delivery, e.g. of substance P to
CC   brain tumours for induction of apoptosis. Unlike the neurotoxins, (I) are
CC   not toxic or immunogenic and are more readily available. Their
CC   therapeutic effect lasts for several days or weeks, so lower doses or
CC   less frequent treatments are required.
XX
SQ   Sequence   206 AA;

  Query Match            100.0%;  Score 39;  DB 18;  Length 206;
  Best Local Similarity  100.0%;  Pred. No. 3.9;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 QIDRIMEK 8
          ||||||||
Db    177 QIDRIMEK 184


RESULT 15
AAW79198
ID   AAW79198 standard; Protein; 206 AA.
XX
AC   AAW79198;
XX
DT   25-NOV-1998  (first entry)
XX
DE   Mouse SNAP-25 polypeptide.
XX
KW   Hrs-2 polypeptide; ATP-preferring nucleotidase; SNAP-25; vesicle docking;
KW   calcium-regulated secretion; secretory vesicle; secretory process; brain;
KW   neurotransmitter release; presynaptic membrane; CNS disorder; depression;
KW   Parkinson's disease; endocrine system; hormonal imbalance; cell division;
KW   thought disorder; schizophrenia; degenerative disorder; anaesthesia; rat;
KW   immune system; antigen processing; immunomodulator; viral processing;
KW   central nervous system; vesicular release; affective disorder; human;
KW   anti-tumour application; membrane trafficking regulation; mouse.
XX
OS   Mus sp.
XX
PN   WO9838210-A2.
XX
PD   03-SEP-1998.
XX
PF   26-FEB-1998;   98WO-US03789.
XX
PR   26-FEB-1997;   97US-0039159.
XX
PA   (STRD ) UNIV LELAND STANFORD JUNIOR.
XX
PI   Bean AJ,  Scheller RH;
XX
DR   WPI; 1998-481140/41.
DR   N-PSDB; AAV57558.
XX
PT   New isolated Hrs-2 nucleotidase - used in assays to identify
PT   compounds capable of modulating calcium-regulatory secretion of
PT   secretory vesicles, such as in neurotransmitter release
XX
PS   Claim 16; Pages 42-44; 55pp; English.
XX
CC   This represents a mouse SNAP-25 polypeptide, a component of the protein
CC   polypeptides thought to underlie vesicle docking and fusion. The
CC   invention provides rat and human Hrs-2 polypeptides which are ATP-
CC   preferring nucleotidase that associate with SNAP-25. For identifying a
CC   compound capable of modulating calcium-regulated secretion of secretory
CC   vesicles, a SNAP-25 polypeptide can be contacted with a Hrs-2
CC   polypeptide, in the presence and absence of a test compound. The effect
CC   of the test compound on the extent of binding between the SNAP-25 and
CC   Hrs-2 polypeptides are measured and a compound is identified as effective
CC   if its measured effect on the extent of binding is above a threshold
CC   level. The products can be used for identifying drugs capable of
CC   affecting secretory processes, such as neurotransmitter release at the
CC   active zones of presynaptic membranes. Such drugs can be used for
CC   treating disorders or conditions of the central nervous system by
CC   selectively enhancing or inhibiting vesicular release in specific areas
CC   of the brain, including affective disorders (e.g. depression), disorders
CC   of thought (e.g. schizophrenia) and degenerative disorders ( Parkinson's
CC   disease), as well as applications such as anaesthesia.  The drugs can
CC   also be used therapeutically in other systems such as the endocrine
CC   system for treatment of hormonal imbalances, the immune system for
CC   intervention in antigen processing, secreted immunomodulators, and viral
CC   processing, as well as anti-tumour applications, such as regulation of
CC   membrane trafficking during rapid cell division.
XX
SQ   Sequence   206 AA;

  Query Match            100.0%;  Score 39;  DB 19;  Length 206;
  Best Local Similarity  100.0%;  Pred. No. 3.9;
  Matches    8;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 QIDRIMEK 8
          ||||||||
```

Db 177 QIDRIMEK 184

Search completed: November 19, 2002, 17:34:27
Job time : 4.35135 secs

GenCore version 5.1.3

OM protein - protein search, using sw model

Run on: November 19, 2002, 17:35:04 ; Search time 22.3125 Seconds
(without alignments)
101.524 Million cell updates/sec

Title: PCT-US02-27145-2_COPY_187_203
Perfect score: 83
Sequence: 1 SNKTRIDEANQRATKML 17

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_101002:*
1: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1980.DAT:*
2: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1981.DAT:*
3: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1982.DAT:*
4: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1983.DAT:*
5: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1984.DAT:*
6: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1985.DAT:*
7: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1986.DAT:*
8: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1987.DAT:*
9: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:*
10: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1989.DAT:*
11: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1990.DAT:*
12: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1991.DAT:*
13: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1992.DAT:*
14: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:*
15: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1994.DAT:*
16: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1995.DAT:*
17: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1996.DAT:*
18: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:*
19: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1998.DAT:*
20: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1999.DAT:*
21: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:*
22: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:*
23: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	83	100.0	17	20	AAY44021	Amino acids 187-20
2	83	100.0	17	20	AAY44057	Human SNAP25 (amin
3	83	100.0	17	23	ABG69065	Human polypeptide
4	83	100.0	19	22	AAB15586	Human SNAP-25 N-te
5	83	100.0	20	18	AAW30100	Neurotransmitter s
6	83	100.0	26	18	AAW30099	Neurotransmitter s
7	83	100.0	37	18	AAW30097	Neurotransmitter s
8	83	100.0	70	17	AAR86823	SNAP-25 residues 1
9	83	100.0	86	22	AAB15584	Human SNAP-25 N-te
10	83	100.0	116	23	AAO15165	Clostridial neurot
11	83	100.0	206	18	AAW30103	Synaptosomal assoc
12	83	100.0	206	19	AAW79198	Mouse SNAP-25 poly
13	83	100.0	206	19	AAW43426	Mouse synaptosomal
14	83	100.0	206	22	AAU00246	Synaptosomal-assoc
15	83	100.0	206	22	AAU00252	SNARE homologue, s
16	83	100.0	206	22	AAU00253	SNARE homologue, s
17	80	96.4	17	20	AAY44038	Human SNAP25 (amin
18	80	96.4	17	20	AAY44063	Human SNAP25 (amin
19	79	95.2	16	20	AAY44069	Human SNAP25 (amin
20	79	95.2	17	20	AAY44047	Human SNAP25 (amin
21	79	95.2	17	20	AAY44050	Human SNAP25 (amin
22	79	95.2	17	20	AAY44052	Human SNAP25 (amin
23	79	95.2	17	20	AAY44059	Human SNAP25 (amin
24	79	95.2	206	22	AAU02640	Synaptosomal-assoc
25	78	94.0	17	20	AAY44039	Human SNAP25 (amin
26	78	94.0	17	20	AAY44045	Human SNAP25 (amin
27	78	94.0	17	20	AAY44049	Human SNAP25 (amin
28	78	94.0	17	20	AAY44062	Human SNAP25 (amin
29	78	94.0	17	20	AAY44070	Human SNAP25 (amin
30	77	92.8	17	20	AAY44022	Human SNAP25 (amin
31	77	92.8	17	20	AAY44040	Human SNAP25 (amin
32	77	92.8	17	20	AAY44044	Human SNAP25 (amin
33	77	92.8	17	20	AAY44046	Human SNAP25 (amin
34	77	92.8	17	20	AAY44048	Human SNAP25 (amin
35	77	92.8	17	20	AAY44051	Human SNAP25 (amin
36	77	92.8	17	20	AAY44053	Human SNAP25 (amin
37	77	92.8	17	20	AAY44054	Human SNAP25 (amin
38	77	92.8	17	20	AAY44056	Human SNAP25 (amin
39	77	92.8	17	20	AAY44064	Human SNAP25 (amin
40	77	92.8	17	20	AAY44065	Human SNAP25 (amin
41	77	92.8	17	20	AAY44066	Human SNAP25 (amin
42	77	92.8	24	23	AAO15162	Clostridial neurot
43	77	92.8	116	23	AAO15166	Clostridial neurot
44	77	92.8	203	22	AAU02636	Synaptosomal-assoc
45	77	92.8	206	22	AAU00259	Synaptosomal-assoc

ALIGNMENTS

RESULT 1
AAY44021
ID AAY44021 standard; peptide; 17 AA.
XX
AC AAY44021;
XX
DT 18-JAN-2000 (first entry)
XX
DE Amino acids 187-203 of human SNAP25.
XX
KW Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW hydrolysis; amino group.
XX
OS Homo sapiens.
XX
PN US5965699-A.
XX
PD 12-OCT-1999.
XX
PF 06-NOV-1996; 96US-0743894.
XX
PR 06-NOV-1996; 96US-0743894.
XX
PA (USSA) US SEC OF ARMY.
XX
PI Bostian KA, Schmidt JJ;
XX
DR WPI; 1999-579939/49.
XX
PT Quantitation of type A botulinum toxin -
XX
PS Claim 1; Column 4; 28pp; English.

XX
CC The invention relates to an enzymatic assay for the quantitation of
CC type A botulinum toxin, by determining the proteolytic activity of
CC botulinum neurotoxin type A using fluorescamine detection. The method
CC comprises adding an analogue (e.g. AAY44022-Y44076) of this peptide
CC (which represents amino acids 187-203 of the human synaptosomal protein
CC SNAP25) to a sample containing the botulinum toxin A so that hydrolysis
CC of the peptide is initiated, then stopping hydrolysis of the peptide at
CC different time points; and measuring the amount of hydrolysis at each
CC time point by combining with a label capable of detecting free amino
CC groups resulting from the hydrolysis. The amount of botulinum toxin A
CC present in the sample is determined by comparing measurements with the
CC amount of label produced from a known concentration of toxin measured
CC under similar conditions. The method is useful for the quantitation of
CC type A botulinum toxin.
XX
SQ Sequence 17 AA;

Query Match 100.0%; Score 83; DB 20; Length 17;
Best Local Similarity 100.0%; Pred. No. 9.4e-08;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 SNKTRIDEANQRATKML 17
||||||||||||||||||
Db 1 SNKTRIDEANQRATKML 17

RESULT 2
AAY44057
ID AAY44057 standard; peptide; 17 AA.
XX
AC AAY44057;
XX
DT 18-JAN-2000 (first entry)
XX
DE Human SNAP25 (amino acids 187-203) analogue #36.
XX
KW Enzymatic assay; quantitation; type A botulinum neurotoxin; proteolysis;
KW fluorescamine; detection; human; synaptosomal protein; SNAP25;
KW hydrolysis; amino group.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN US5965699-A.
XX
PD 12-OCT-1999.
XX
PF 06-NOV-1996; 96US-0743894.
XX
PR 06-NOV-1996; 96US-0743894.
XX
PA (USSA) US SEC OF ARMY.
XX
PI Bostian KA, Schmidt JJ;
XX
DR WPI; 1999-579939/49.
XX
PT Quantitation of type A botulinum toxin -
XX
PS Disclosure; Column 9; 28pp; English.
XX
CC The invention relates to an enzymatic assay for the quantitation of
CC type A botulinum toxin, by determining the proteolytic activity of
CC botulinum neurotoxin type A using fluorescamine detection. Botulinum
CC toxin A has been shown to cleave the synaptosomal neurotransmitter
CC peptide SNAP25 between residues 197-198. The method comprises adding
CC an analogue (e.g. AAY44022-Y44076) of the SNAP25 peptide (AAY44021,
CC amino acids 187-203 of human SNAP25) to a sample containing the
CC botulinum toxin A so that hydrolysis of the peptide is initiated, then
CC stopping hydrolysis of the peptide at different time points; and
CC measuring the amount of hydrolysis at each time point by combining with a
CC label capable of detecting free amino groups resulting from the
CC hydrolysis. The amount of botulinum toxin A present in the sample is
CC determined by comparing measurements with the amount of label produced
CC from a known concentration of toxin measured under similar conditions.
CC The method is useful for the quantitation of type A botulinum toxin.
XX
SQ Sequence 17 AA;

Query Match 100.0%; Score 83; DB 20; Length 17;
Best Local Similarity 100.0%; Pred. No. 9.4e-08;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 SNKTRIDEANQRATKML 17
||||||||||||||||||
Db 1 SNKTRIDEANQRATKML 17

RESULT 3
ABG69065
ID ABG69065 standard; Peptide; 17 AA.
XX
AC ABG69065;
XX
DT 07-OCT-2002 (first entry)
XX
DE Human polypeptide C-terminal fragment.
XX
KW Botulinum neurotoxin light chain; BoNT LC; botulism; dystonia; pain;
KW spasticity; ocular motility; facial dyskinesia; stiff-person syndrome;
KW bladder dysfunction; segmental myoclonus; hyperkinetic disorder; human;
KW cosmetic treatment; facial wrinkle; cerebral palsy; analgesic; relaxant;
KW lower motor neuron hyperactivity; autonomic nerve function; muscular;
KW immunostimulant; antibacterial.
XX
OS Homo sapiens.
XX
PN WO200236758-A2.
XX
PD 10-MAY-2002.
XX
PF 06-NOV-2001; 2001WO-US47230.
XX
PR 06-NOV-2000; 2000US-246774P.
PR 20-JUL-2001; 2001US-0910186.
PR 09-AUG-2001; 2001US-311966P.
XX
PA (USSA) US ARMY MEDICAL RES & MATERIAL COMMAND.
XX
PI Smith LA, Jensen M;
XX
DR WPI; 2002-575192/61.
XX
PT Novel nucleic acid molecule encoding botulinum neurotoxin light chain
PT serotype A, useful for producing the neurotoxin for vaccination against
PT botulism, comprises sequence expressible in host other than Clostridium
PT -
XX
PS Example 25; Page 62; 166pp; English.
XX
CC The invention relates to a nucleic acid molecule encoding a botulinum
CC neurotoxin light chain (BoNT LC) serotype A, where the DNA has a sequence
CC that is expressible in a host organism other than Clostridium, or has a
CC total A+T content that is less than about 70% The BoNT LC protein is
CC useful in vaccination against botulism, for eliciting protective immunity
CC in a mammal, for treating dystonias, spasticity, pain, ocular motility,
CC facial dyskinesias, stiff-person syndrome, bladder dysfunction, segmental
CC myoclonus, hyperkinetic disorders, cosmetic treatment of facial wrinkles,
CC conditions characterised by hyperactivity of the lower motor neuron, and
CC to control autonomic nerve function or tiptoe-walking due to stiff
CC muscles common in children with cerebral palsy. The sequences are also
CC useful for screening for botulinum neurotoxin inhibitors. This sequence
CC represents a human polypeptide C-terminal fragment, used in the scope of
CC the invention.
XX

```
SQ   Sequence   17 AA;

  Query Match           100.0%;  Score 83;  DB 23;  Length 17;
  Best Local Similarity  100.0%;  Pred. No. 9.4e-08;
  Matches   17;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 SNKTRIDEANQRATKML 17
          |||||||||||||||||
Db      1 SNKTRIDEANQRATKML 17


RESULT 4
AAB15586
ID   AAB15586 standard; peptide; 19 AA.
XX
AC   AAB15586;
XX
DT   02-MAR-2001  (first entry)
XX
DE   Human SNAP-25 N-terminal peptide #6.
XX
KW   Dermatological; neuroprotective; relaxant; neuronal exocytosis modulator;
KW   SNAP-25; synaptosomal-associated protein 25; facial wrinkle; asymmetry;
KW   neurodegenerative disorder.
XX
OS   Homo sapiens.
XX
PN   WO200064932-A1.
XX
PD   02-NOV-2000.
XX
PF   18-FEB-2000; 2000WO-ES00058.
XX
PR   23-APR-1999;   99ES-0000844.
XX
PA   (LIPO-) LIPOTEC SA.
XX
PI   Blanes Mira MC,  Llobregat Hernandez MM,  Gil Tebar AI;
PI   Fernandez Ballester GJ,  Planell Cases RM,  Ferrer Montiel AV;
PI   Viniegra Bover S,  Gutierrez Perez LM,  Carbonell Castell T;
PI   Perez Paya E;
XX
DR   WPI; 2001-007091/01.
XX
PT   New peptides containing amino acid sequences from known proteins for
PT   treatment of neurological disorders  -
XX
PS   Claim 17; Page 34; 40pp; Spanish.
XX
CC   The invention relates to new peptides comprising 3-30 contiguous amino
CC   acids from the N-terminus of the protein SNAP-25
CC   (synaptosomal-associated protein 25). The peptides AAB15581-B15586
CC   represent examples of the peptides of the invention. The peptides have
CC   neuronal exocytosis inhibitory activity and are used for treatment of
CC   facial wrinkles and asymmetry and pathological neuronal
CC   exocytosis-mediated pathological disorders and alterations manifested
CC   e.g. by spasms and neurological and neurodegenerative disorders.
XX
SQ   Sequence   19 AA;

  Query Match           100.0%;  Score 83;  DB 22;  Length 19;
  Best Local Similarity  100.0%;  Pred. No. 1.1e-07;
  Matches   17;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 SNKTRIDEANQRATKML 17
          |||||||||||||||||
Db      3 SNKTRIDEANQRATKML 19


RESULT 5
AAW30100
ID   AAW30100 standard; peptide; 20 AA.
XX
AC   AAW30100;
XX
DT   06-APR-1998  (first entry)
XX
DE   Neurotransmitter secretion inhibitor #4.
XX
KW   Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW   excitation-secretory uncoupling peptide; catecholamine secretion;
KW   bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW   synaptosomal associated protein; SNAP-25.
XX
OS   Homo sapiens.
XX
PN   WO9734620-A1.
XX
PD   25-SEP-1997.
XX
PF   18-MAR-1997;   97WO-US04393.
XX
PR   18-MAR-1996;   96US-0013599.
XX
PA   (REGC ) UNIV CALIFORNIA.
XX
PI   Montal M;
XX
DR   WPI; 1997-479986/44.
XX
PT   Excitation-secretory uncoupling peptide(s) for inhibiting
PT   neurotransmitter release - used particularly for treating muscle
PT   spasticity, and for delivering drugs specifically to neural cells
XX
PS   Claim 14; Page 32; 61pp; English.
XX
CC   This sequence corresponds to residues 187-206 of the human 25 kD
CC   synaptosomal associated protein (SNAP-25), and is a inhibitory agent of
CC   the invention. The agents of the invention inhibit secretion of
CC   neurotransmitter from neuronal cells and is an excitation-secretory
CC   uncoupling peptide (I) of at least 20 amino acids (aa) all of which
CC   correspond substantially to any one of AAW30097-W30102, or more
CC   generally any (I) that inhibits 50% of catecholamine secretion from
CC   bovine chromaffin cells at a concentration of 10 microM, especially 0.25
CC   microM, or less. (I) are used, as a replacement for Clostridium toxin, to
CC   inhibit release of neurotransmitters from synaptic vesicles, specifically
CC   for reducing muscle spasticity. Also (I) may be labelled to allow in
CC   vivo imaging of intracellular distribution of (I). Compounds for
CC   delivering the drug to neural cells provide targeted drug delivery, e.g.
CC   of substance P to brain tumours for induction of apoptosis. Unlike the
CC   neurotoxins, (I) are not toxic or immunogenic and are more readily
CC   available. Their therapeutic effect lasts for several days or weeks, so
CC   lower doses or less frequent treatments are required.
XX
SQ   Sequence   20 AA;

  Query Match           100.0%;  Score 83;  DB 18;  Length 20;
  Best Local Similarity  100.0%;  Pred. No. 1.1e-07;
  Matches   17;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 SNKTRIDEANQRATKML 17
          |||||||||||||||||
Db      1 SNKTRIDEANQRATKML 17


RESULT 6
AAW30099
ID   AAW30099 standard; peptide; 26 AA.
XX
AC   AAW30099;
XX
DT   06-APR-1998  (first entry)
XX
DE   Neurotransmitter secretion inhibitor #3.
XX
KW   Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
```

KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle
PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Claim 13; Page 31; 61pp; English.
XX
CC This sequence corresponds to residues 181-206 of the human 25 kD
CC synaptosomal associated protein (SNAP-25), and is a inhibitory agent of
CC the invention. The agents of the invention inhibit secretion of
CC neurotransmitter from neuronal cells and is an excitation-secretory
CC uncoupling peptide (I) of at least 20 amino acids (aa) all of which
CC correspond substantially to any one of AAW30097-W30102, or more
CC generally any (I) that inhibits 50% of catecholamine secretion from
CC bovine chromaffin cells at a concentration of 10 microM, especially 0.25
CC microM, or less. (I) are used, as a replacement for Clostridium toxin, to
CC inhibit release of neurotransmitters from synaptic vesicles, specifically
CC for reducing muscle spasticity. Also (I) may be labelled to allow in
CC vivo imaging of intracellular distribution of (I). Compounds for
CC delivering the drug to neural cells provide targeted drug delivery, e.g.
CC of substance P to brain tumours for induction of apoptosis. Unlike the
CC neurotoxins, (I) are not toxic or immunogenic and are more readily
CC available. Their therapeutic effect lasts for several days or weeks, so
CC lower doses or less frequent treatments are required.
XX
SQ Sequence 26 AA;

Query Match 100.0%; Score 83; DB 18; Length 26;
Best Local Similarity 100.0%; Pred. No. 1.5e-07;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 SNKTRIDEANQRATKML 17
||||||||||||||||||
Db 7 SNKTRIDEANQRATKML 23

RESULT 7
AAW30097
ID AAW30097 standard; peptide; 37 AA.
XX
AC AAW30097;
XX
DT 06-APR-1998 (first entry)
XX
DE Neurotransmitter secretion inhibitor #1.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PW WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle
PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Claim 1; Page 30; 61pp; English.
XX
CC This sequence corresponds to residues 170-206 of the human 25 kD
CC synaptosomal associated protein (SNAP-25), and is a inhibitory agent of
CC the invention. The agents of the invention inhibit secretion of
CC neurotransmitter from neuronal cells and is an excitation-secretory
CC uncoupling peptide (I) of at least 20 amino acids (aa) all of which
CC correspond substantially to any one of AAW30097-W30102, or more
CC generally any (I) that inhibits 50% of catecholamine secretion from
CC bovine chromaffin cells at a concentration of 10 microM, especially 0.25
CC microM, or less. (I) are used, as a replacement for Clostridium toxin, to
CC inhibit release of neurotransmitters from synaptic vesicles, specifically
CC for reducing muscle spasticity. Also (I) may be labelled to allow in
CC vivo imaging of intracellular distribution of (I). Compounds for
CC delivering the drug to neural cells provide targeted drug delivery, e.g.
CC of substance P to brain tumours for induction of apoptosis. Unlike the
CC neurotoxins, (I) are not toxic or immunogenic and are more readily
CC available. Their therapeutic effect lasts for several days or weeks, so
CC lower doses or less frequent treatments are required.
XX
SQ Sequence 37 AA;

Query Match 100.0%; Score 83; DB 18; Length 37;
Best Local Similarity 100.0%; Pred. No. 2.3e-07;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 SNKTRIDEANQRATKML 17
||||||||||||||||||
Db 18 SNKTRIDEANQRATKML 34

RESULT 8
AAR86823
ID AAR86823 standard; Peptide; 70 AA.
XX
AC AAR86823;
XX
DT 15-AUG-1996 (first entry)
XX
DE SNAP-25 residues 137-206.
XX
KW VAMP; vesicle-associated membrane protein; SNAP-25; syntaxin;
KW neurotransmitter; neurotoxin; botulinum; botulism; cleavage;
KW substrate; antibody; detection; assay.
XX
OS Synthetic.
XX
PN WO9533850-A1.
XX
PD 14-DEC-1995.
XX
PF 02-JUN-1995; 95WO-GB01279.
XX
PR 03-JUN-1994; 94GB-0011138.
XX
PA (CAMR-) CAMR CENT APPLIED MICROBIOLOGY & RES.

PA (MICR-) MICROBIOLOGICAL RES AUTHORITY.
XX
PI Hallis B, James BAF, Quinn CP, Shone CC;
XX
DR WPI; 1996-040249/04.
XX
PT Assay for botulinum or tetanus toxin - by combining test cpd. with
PT substrate which is cleaved by the toxin, and antibody specific for
PT the cleaved but not uncleaved substrate
XX
PS Example 4; Page 19; 48pp; English.
XX
CC The botulinum neurotoxins possess highly specific zinc-endopeptidase
CC activities within their light sub-units. Depending on the neurotoxin
CC type these act to cleave small proteins within the nerve cell which are
CC involved in neurotransmitter release. Antibodies are used in assays
CC which detect cleaved but not uncleaved substrate. Assays for botulinum
CC types A and E use the present sequence as a substrate. The sequence is
CC SNAP-25 protein, residues 137-206.
XX
SQ Sequence 70 AA;

Query Match 100.0%; Score 83; DB 17; Length 70;
Best Local Similarity 100.0%; Pred. No. 4.6e-07;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 SNKTRIDEANQRATKML 17
||||||||||||||||||
Db 51 SNKTRIDEANQRATKML 67

RESULT 9
AAB15584
ID AAB15584 standard; peptide; 86 AA.
XX
AC AAB15584;
XX
DT 02-MAR-2001 (first entry)
XX
DE Human SNAP-25 N-terminal peptide #4.
XX
KW Dermatological; neuroprotective; relaxant; neuronal exocytosis modulator;
KW SNAP-25; synaptosomal-associated protein 25; facial wrinkle; asymmetry;
KW neurodegenerative disorder.
XX
OS Homo sapiens.
XX
PN WO200064932-A1.
XX
PD 02-NOV-2000.
XX
PF 18-FEB-2000; 2000WO-ES00058.
XX
PR 23-APR-1999; 99ES-0000844.
XX
PA (LIPO-) LIPOTEC SA.
XX
PI Blanes Mira MC, Llobregat Hernandez MM, Gil Tebar AI;
PI Fernandez Ballester GJ, Planell Cases RM, Ferrer Montiel AV;
PI Viniegra Bover S, Gutierrez Perez LM, Carbonell Castell T;
PI Perez Paya E;
XX
DR WPI; 2001-007091/01.
XX
PT New peptides containing amino acid sequences from known proteins for
PT treatment of neurological disorders -
XX
PS Claim 16; Page 32-33; 40pp; Spanish.
XX
CC The invention relates to new peptides comprising 3-30 contiguous amino
CC acids from the N-terminus of the protein SNAP-25
CC (synaptosomal-associated protein 25). The peptides AAB15581-B15586
CC represent examples of the peptides of the invention. The peptides have
CC neuronal exocytosis inhibitory activity and are used for treatment of
CC facial wrinkles and asymmetry and pathological neuronal
CC exocytosis-mediated pathological disorders and alterations manifested
CC e.g. by spasms and neurological and neurodegenerative disorders.
XX
SQ Sequence 86 AA;

Query Match 100.0%; Score 83; DB 22; Length 86;
Best Local Similarity 100.0%; Pred. No. 5.8e-07;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 SNKTRIDEANQRATKML 17
||||||||||||||||||
Db 67 SNKTRIDEANQRATKML 83

RESULT 10
AAO15165
ID AAO15165 standard; peptide; 116 AA.
XX
AC AAO15165;
XX
DT 02-SEP-2002 (first entry)
XX
DE Clostridial neurotoxin protease substrate peptide 4.
XX
KW Clostridial neurotoxin substrate; botulinum neurotoxin substrate; FRET;
KW fluorescence resonant energy transfer assay; quenched-signal;
KW clostridial neurotoxin detection; food.
XX
OS Unidentified.
XX
FH Key Location/Qualifiers
FT Modified-site 1
FT /note= "S-fluoresceinyl-cysteine"
FT Cleavage-site 89..90
FT /note= "The peptide is cleaved between these two
FT residues by type E Clostridium botulinum neurotoxin"
FT Cleavage-site 106..107
FT /note= "The peptide is cleaved between these two
FT residues by type A Clostridium botulinum neurotoxin"
XX
PN WO200225284-A2.
XX
PD 28-MAR-2002.
XX
PF 25-SEP-2001; 2001WO-US30188.
XX
PR 25-SEP-2000; 2000US-235050P.
XX
PA (USME-) US MEDICAL RES INST INFECTIOUS DISEASES.
XX
PI Schmidt JJ, Stafford RG;
XX
DR WPI; 2002-499829/53.
XX
PT Substrate useful in e.g. an assay for the protease activity of
PT clostridial neurotoxin, comprises modified peptide or protein -
XX
PS Claim 22; Page 16; 48pp; English.
XX
CC The invention comprises clostridial neurotoxin substrate peptides which
CC can serve as fluorescence resonant energy transfer assay (FRET) or
CC quenched-signal substrates in assays for the proteolytic activities of
CC clostridial neurotoxins. The invention further comprises Clostridium
CC botulinum neurotoxin substrate peptides that can serve as immobilised
CC substrates (i.e. bound to a solid phase) in assays for the proteolytic
CC activities of clostridial neurotoxins. The clostridial (including the
CC Clostridium botulinum) neurotoxin substrate peptides are useful for
CC detecting the presence of clostridial neurotoxins in a sample (e.g. food
CC or an environmental sample). The present amino acid sequence represents a
CC clostridial neurotoxin substrate peptide of the invention.
XX

```
SQ   Sequence   116 AA;

  Query Match             100.0%;  Score 83;  DB 23;  Length 116;
  Best Local Similarity   100.0%;  Pred. No. 8.2e-07;
  Matches   17;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 SNKTRIDEANQRATKML 17
           |||||||||||||||||
Db      96 SNKTRIDEANQRATKML 112


RESULT 11
AAW30103
ID   AAW30103 standard; peptide; 206 AA.
XX
AC   AAW30103;
XX
DT   06-APR-1998  (first entry)
XX
DE   Synaptosomal associated protein.
XX
KW   Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW   excitation-secretory uncoupling peptide; catecholamine secretion;
KW   bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW   synaptosomal associated protein; SNAP-25.
XX
OS   Homo sapiens.
XX
PN   WO9734620-A1.
XX
PD   25-SEP-1997.
XX
PF   18-MAR-1997;   97WO-US04393.
XX
PR   18-MAR-1996;   96US-0013599.
XX
PA   (REGC ) UNIV CALIFORNIA.
XX
PI   Montal M;
XX
DR   WPI; 1997-479986/44.
XX
PT   Excitation-secretory uncoupling peptide(s) for inhibiting
PT   neuro:transmitter release - used particularly for treating muscle
PT   spasticity, and for delivering drugs specifically to neural cells
XX
PS   Disclosure; Page 27-28; 61pp; English.
XX
CC   This sequence represents the human 25 kD synaptosomal associated protein
CC   (SNAP-25), which is an inhibitory agent of the invention. The agents of
CC   the invention inhibit secretion of neurotransmitter from neuronal cells
CC   and is an excitation-secretory uncoupling peptide (I) of at least 20
CC   amino acids (aa) all of which correspond substantially to any one of
CC   AAW30097-W30102, or more generally any (I) that inhibits 50% of
CC   catecholamine secretion from bovine chromaffin cells at a concentration
CC   of 10 microM, especially 0.25 microM, or less. (I) are used, as a
CC   replacement for Clostridium toxin, to inhibit release of
CC   neurotransmitters from synaptic vesicles, specifically for reducing
CC   muscle spasticity. Also (I) may be labelled to allow in vivo imaging of
CC   intracellular distribution of (I). Compounds for delivering the drug to
CC   neural cells provide targeted drug delivery, e.g. of substance P to
CC   brain tumours for induction of apoptosis. Unlike the neurotoxins, (I) are
CC   not toxic or immunogenic and are more readily available. Their
CC   therapeutic effect lasts for several days or weeks, so lower doses or
CC   less frequent treatments are required.
XX
SQ   Sequence   206 AA;

  Query Match             100.0%;  Score 83;  DB 18;  Length 206;
  Best Local Similarity   100.0%;  Pred. No. 1.6e-06;
  Matches   17;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 SNKTRIDEANQRATKML 17
           |||||||||||||||||
Db     187 SNKTRIDEANQRATKML 203


RESULT 12
AAW79198
ID   AAW79198 standard; Protein; 206 AA.
XX
AC   AAW79198;
XX
DT   25-NOV-1998  (first entry)
XX
DE   Mouse SNAP-25 polypeptide.
XX
KW   Hrs-2 polypeptide; ATP-preferring nucleotidase; SNAP-25; vesicle docking;
KW   calcium-regulated secretion; secretory vesicle; secretory process; brain;
KW   neurotransmitter release; presynaptic membrane; CNS disorder; depression;
KW   Parkinson's disease; endocrine system; hormonal imbalance; cell division;
KW   thought disorder; schizophrenia; degenerative disorder; anaesthesia; rat;
KW   immune system; antigen processing; immunomodulator; viral processing;
KW   central nervous system; vesicular release; affective disorder; human;
KW   anti-tumour application; membrane trafficking regulation; mouse.
XX
OS   Mus sp.
XX
PN   WO9838210-A2.
XX
PD   03-SEP-1998.
XX
PF   26-FEB-1998;   98WO-US03789.
XX
PR   26-FEB-1997;   97US-0039159.
XX
PA   (STRD ) UNIV LELAND STANFORD JUNIOR.
XX
PI   Bean AJ,  Scheller RH;
XX
DR   WPI; 1998-481140/41.
DR   N-PSDB; AAV57558.
XX
PT   New isolated Hrs-2 nucleotidase - used in assays to identify
PT   compounds capable of modulating calcium-regulatory secretion of
PT   secretory vesicles, such as in neurotransmitter release
XX
PS   Claim 16; Pages 42-44; 55pp; English.
XX
CC   This represents a mouse SNAP-25 polypeptide, a component of the protein
CC   polypeptides thought to underlie vesicle docking and fusion. The
CC   invention provides rat and human Hrs-2 polypeptides which are ATP-
CC   preferring nucleotidase that associate with SNAP-25. For identifying a
CC   compound capable of modulating calcium-regulated secretion of secretory
CC   vesicles, a SNAP-25 polypeptide can be contacted with a Hrs-2
CC   polypeptide, in the presence and absence of a test compound. The effect
CC   of the test compound on the extent of binding between the SNAP-25 and
CC   Hrs-2 polypeptides are measured and a compound is identified as effective
CC   if its measured effect on the extent of binding is above a threshold
CC   level. The products can be used for identifying drugs capable of
CC   affecting secretory processes, such as neurotransmitter release at the
CC   active zones of presynaptic membranes. Such drugs can be used for
CC   treating disorders or conditions of the central nervous system by
CC   selectively enhancing or inhibiting vesicular release in specific areas
CC   of the brain, including affective disorders (e.g. depression), disorders
CC   of thought (e.g. schizophrenia) and degenerative disorders ( Parkinson's
CC   disease), as well as applications such as anaesthesia.  The drugs can
CC   also be used therapeutically in other systems such as the endocrine
CC   system for treatment of hormonal imbalances, the immune system for
CC   intervention in antigen processing, secreted immunomodulators, and viral
CC   processing, as well as anti-tumour applications, such as regulation of
CC   membrane trafficking during rapid cell division.
XX
SQ   Sequence   206 AA;

  Query Match             100.0%;  Score 83;  DB 19;  Length 206;
```

Best Local Similarity 100.0%; Pred. No. 1.6e-06;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy       1 SNKTRIDEANQRATKML 17
           |||||||||||||||||
Db     187 SNKTRIDEANQRATKML 203
```

RESULT 13
AAW43426
ID AAW43426 standard; Protein; 206 AA.
XX
AC AAW43426;
XX
DT 27-APR-1998 (first entry)
XX
DE Mouse synaptosomal-associated protein-25.
XX
KW Binding domain; mouse; syntaxin; synaptosomal-associated protein; CNS;
KW neurotransmitter; presynaptic membrane; central nervous system; tumour;
KW neurodegenerative disease; hormonal disorder; immunological disorder.
XX
OS Mus sp.
XX
PN US5693476-A.
XX
PD 02-DEC-1997.
XX
PF 24-FEB-1995; 95US-0393985.
XX
PR 24-FEB-1995; 95US-0393985.
XX
PA (STRD) UNIV LELAND STANFORD JUNIOR.
XX
PI Scheller RH;
XX
DR WPI; 1998-031743/03.
DR N-PSDB; AAV01554.
XX
PT Screening assay for modulators of syntaxin binding - using peptide
PT comprising binding site of syntaxin, for identifying drugs useful
PT for treating CNS disorders, neuro-degenerative diseases, etc
XX
PS Disclosure; Column 67-72; 57pp; English.
XX
CC This amino acid sequence represents the mouse synaptosomal-associated
CC protein of 25 kD (SNAP-25). The invention relates to a method for
CC identifying a compound capable of affecting the binding of a
CC syntaxin-binding protein (SBP), e.g. SNAP-25, alpha-SNAP, n-sec1 or VAMP,
CC to syntaxin. The method comprises measuring the effect of the test
CC compound on the extent of binding between the SBP and the SBP-binding
CC site on syntaxin. The method can be used for identifying drugs capable
CC of inhibiting or stimulating neurotransmitter release at the active zones
CC of presynaptic membranes, which may be useful for treating CNS disorders,
CC affective or psychotic disorders, neurodegenerative diseases, hormonal or
CC immunological disorders or tumours.
XX
SQ Sequence 206 AA;

Query Match 100.0%; Score 83; DB 19; Length 206;
Best Local Similarity 100.0%; Pred. No. 1.6e-06;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy       1 SNKTRIDEANQRATKML 17
           |||||||||||||||||
Db     187 SNKTRIDEANQRATKML 203
```

RESULT 14
AAU00246
ID AAU00246 standard; Protein; 206 AA.
XX
AC AAU00246;
XX
DT 12-SEP-2001 (first entry)
XX
DE Synaptosomal-associated protein, SNAP25.
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; mutagenic; PCR primer; mouse;
KW N-ethylmaleimide-sensitive fusion protein;
KW soluble NSF-attachment protein receptor.
XX
OS Mus sp.
XX
XX
FH Key Location/Qualifiers
FT Cleavage-site 180..181
FT /note= "Peptide bond susceptible to cleavage by
FT clostridial neurotoxin"
FT Cleavage-site 197..198
FT /note= "Peptide bonds susceptible to cleavage by
FT clostridial neurotoxin"
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Disclosure; Fig 8; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25. The sequence was used to
CC create SNAP-25 double/single point mutants and C-terminal deletion
CC mutants used in a new method of treating a patient suffering from
CC poisoning or at risk of poisoning by a clostridial toxin, comprising
CC supplying a SNARE (soluble (N-ethylmaleimide-sensitive fusion protein)-
CC attachment protein receptor) to a cell of the patient, where the SNARE is
CC resistant to proteolysis by the toxin (toxin-resistant SNARE) and/or is
CC capable of inhibiting the toxin (toxin-inhibitory SNARE). The protein can
CC be used in a method of treating a patient in need of inhibition of SNARE-
CC dependent exocytosis from a cell capable of performing SNARE-dependent
CC exocytosis, comprises supplying a fragment, variant, fusion or derivative
CC of a SNARE or an inhibitory SNARE to the cell of the patient. The toxin
CC resistant or toxin inhibitory SNARE or a recombinant polynucleotide
CC encoding the SNARE is useful in the manufacture of a medicament for the
CC treatment of a patient suffering from poisoning or at risk of poisoning
CC by clostridial toxin, e.g. from botulism or tetanus. The fragment,
CC variant, fusion or derivative of a SNARE or of an inhibitory SNARE, or a
CC recombinant polynucleotide encoding either of these SNARE polypeptides
CC are useful in the manufacture of medicament for the treatment of a
CC patient in need of inhibition of SNARE-dependent exocytosis from a cell
CC capable of performing SNARE-dependent exocytosis. The method of treatment
CC is relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
XX
SQ Sequence 206 AA;

Query Match 100.0%; Score 83; DB 22; Length 206;
Best Local Similarity 100.0%; Pred. No. 1.6e-06;
Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 SNKTRIDEANQRATKML 17
          |||||||||||||||||
Db    187 SNKTRIDEANQRATKML 203
```

RESULT 15
AAU00252
ID AAU00252 standard; Protein; 206 AA.
XX
AC AAU00252;
XX
DT 12-SEP-2001 (first entry)
XX
DE SNARE homologue, synaptosomal-associated protein, hSNAP25a.
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; hSNAP25a; human;
KW N-ethylmaleimide-sensitive fusion;
KW soluble NSF-attachment protein receptor.
XX
OS Homo sapiens.
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
DR N-PSDB; AAS00369.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Disclosure; Fig 8; 131pp; English.
XX
CC The sequence represents the amino acid sequence of SNARE homologue,
CC synaptosomal-associated membrane protein, hSNAP25a, used during analysis
CC of SNAP-25. SNAP-25 mutants were used in a new method of treating a
CC patient suffering from poisoning or at risk of poisoning by a clostridial
CC toxin, comprising supplying a SNARE (soluble (N-ethylmaleimide-sensitive
CC fusion protein)-attachment protein receptor) to a cell of the patient,
CC where the SNARE is resistant to proteolysis by the toxin (toxin-resistant
CC SNARE) and/or is capable of inhibiting the toxin (toxin-inhibitory
CC SNARE). The protein can be used in a method of treating a patient in need
CC of inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis, comprises supplying a fragment,
CC variant, fusion or derivative of a SNARE or an inhibitory SNARE to the
CC cell of the patient. The toxin resistant or toxin inhibitory SNARE or a
CC recombinant polynucleotide encoding the SNARE is useful in the
CC manufacture of a medicament for the treatment of a patient suffering from
CC poisoning or at risk of poisoning by clostridial toxin, e.g. from
CC botulism or tetanus. The fragment, variant, fusion or derivative of a
CC SNARE or of an inhibitory SNARE, or a recombinant polynucleotide encoding
CC either of these SNARE polypeptides are useful in the manufacture of
CC medicament for the treatment of a patient in need of inhibition of SNARE-
CC dependent exocytosis from a cell capable of performing SNARE-dependent
CC exocytosis. The method of treatment is relatively fast, thus
CC alleviating the symptoms when most severe and taking the patient out of
CC critical state.
XX
SQ Sequence 206 AA;

• Query Match 100.0%; Score 83; DB 22; Length 206;
  Best Local Similarity 100.0%; Pred. No. 1.6e-06;

  Matches 17; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 SNKTRIDEANQRATKML 17
          |||||||||||||||||
Db    187 SNKTRIDEANQRATKML 203
```

Search completed: November 19, 2002, 17:39:13
Job time : 22.3125 secs

GenCore version 5.1.3

OM protein - protein search, using sw model

Run on: November 19, 2002, 17:35:04 ; Search time 40.6875 Seconds
(without alignments)
101.524 Million cell updates/sec

Title: PCT-US02-27145-2_COPY_156_186
Perfect score: 158
Sequence: 1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_101002:*
1: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1980.DAT:*
2: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1981.DAT:*
3: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1982.DAT:*
4: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1983.DAT:*
5: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1984.DAT:*
6: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1985.DAT:*
7: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1986.DAT:*
8: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1987.DAT:*
9: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1988.DAT:*
10: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1989.DAT:*
11: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1990.DAT:*
12: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1991.DAT:*
13: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1992.DAT:*
14: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1993.DAT:*
15: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1994.DAT:*
16: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1995.DAT:*
17: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1996.DAT:*
18: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1997.DAT:*
19: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1998.DAT:*
20: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA1999.DAT:*
21: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2000.DAT:*
22: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2001.DAT:*
23: /SIDS2/gcgdata/geneseq/geneseqp-embl/AA2002.DAT:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	158	100.0	70	17	AAR86823	SNAP-25 residues 1
2	158	100.0	116	23	AAO15165	Clostridial neurot
3	158	100.0	116	23	AAO15166	Clostridial neurot
4	158	100.0	198	22	AAU00255	Synaptosomal-assoc
5	158	100.0	199	22	AAU00263	Synaptosomal-assoc
6	158	100.0	200	22	AAU00264	Synaptosomal-assoc
7	158	100.0	201	22	AAU02637	Synaptosomal-assoc
8	158	100.0	202	22	AAU00265	Synaptosomal-assoc
9	158	100.0	203	22	AAU02636	Synaptosomal-assoc
10	158	100.0	206	18	AAW30103	Synaptosomal assoc
11	158	100.0	206	19	AAW79198	Mouse SNAP-25 poly
12	158	100.0	206	19	AAW43426	Mouse synaptosomal
13	158	100.0	206	22	AAU00246	Synaptosomal-assoc
14	158	100.0	206	22	AAU00252	SNARE homologue, s
15	158	100.0	206	22	AAU00253	SNARE homologue, s
16	158	100.0	206	22	AAU00256	Synaptosomal-assoc
17	158	100.0	206	22	AAU00257	Synaptosomal-assoc
18	158	100.0	206	22	AAU00258	Synaptosomal-assoc
19	158	100.0	206	22	AAU00259	Synaptosomal-assoc
20	158	100.0	206	22	AAU00260	Synaptosomal-assoc
21	158	100.0	206	22	AAU00261	Synaptosomal-assoc
22	158	100.0	206	22	AAU00262	Synaptosomal-assoc
23	158	100.0	206	22	AAU00266	Synaptosomal-assoc
24	158	100.0	206	22	AAU02171	Synaptosomal-assoc
25	158	100.0	206	22	AAU02638	Synaptosomal-assoc
26	158	100.0	206	22	AAU02639	Synaptosomal-assoc
27	158	100.0	206	22	AAU02640	Synaptosomal-assoc
28	156	98.7	86	22	AAB15584	Human SNAP-25 N-te
29	148	93.7	49	22	AAM57386	Human brain expres
30	122	77.2	61	22	AAU00248	Synaptosomal-assoc
31	109	69.0	212	22	ABB64447	Drosophila melanog
32	107	67.7	61	22	AAU00247	Synaptosomal-assoc
33	107	67.7	211	22	ABG02947	Novel human diagno
34	107	67.7	211	22	AAU00251	SNARE homologue, s
35	107	67.7	213	21	AAB57140	Human prostate can
36	86	54.4	513	21	AAG32996	Arabidopsis thalia
37	86	54.4	546	21	AAG32995	Arabidopsis thalia
38	86	54.4	714	21	AAG32994	Arabidopsis thalia
39	85	53.8	20	18	AAW30098	Neurotransmitter s
40	85	53.8	37	18	AAW30097	Neurotransmitter s
41	83	52.5	165	21	AAG09028	Arabidopsis thalia
42	83	52.5	165	21	AAG39337	Arabidopsis thalia
43	83	52.5	247	21	AAG09027	Arabidopsis thalia
44	83	52.5	247	21	AAG23785	Arabidopsis thalia
45	83	52.5	247	21	AAG39336	Arabidopsis thalia

ALIGNMENTS

RESULT 1
AAR86823
ID AAR86823 standard; Peptide; 70 AA.
XX
AC AAR86823;
XX
DT 15-AUG-1996 (first entry)
XX
DE SNAP-25 residues 137-206.
XX
KW VAMP; vesicle-associated membrane protein; SNAP-25; syntaxin;
KW neurotransmitter; neurotoxin; botulinum; botulism; cleavage;
KW substrate; antibody; detection; assay.
XX
OS Synthetic.
XX
PN WO9533850-A1.
XX
PD 14-DEC-1995.
XX
PF 02-JUN-1995; 95WO-GB01279.
XX
PR 03-JUN-1994; 94GB-0011138.
XX
PA (CAMR-) CAMR CENT APPLIED MICROBIOLOGY & RES.
PA (MICR-) MICROBIOLOGICAL RES AUTHORITY.
XX
PI Hallis B, James BAF, Quinn CP, Shone CC;
XX
DR WPI; 1996-040249/04.
XX
PT Assay for botulinum or tetanus toxin - by combining test cpd. with
PT substrate which is cleaved by the toxin, and antibody specific for

```
PT   the cleaved but not uncleaved substrate
XX
PS   Example 4; Page 19; 48pp; English.
XX
CC   The botulinum neurotoxins possess highly specific zinc-endopeptidase
CC   activities within their light sub-units. Depending on the neurotoxin
CC   type these act to cleave small proteins within the nerve cell which are
CC   involved in neurotransmitter release.  Antibodies are used in assays
CC   which detect cleaved but not uncleaved substrate. Assays for botulinum
CC   types A and E use the present sequence as a substrate. The sequence is
CC   SNAP-25 protein, residues 137-206.
XX
SQ   Sequence   70 AA;

  Query Match             100.0%;  Score 158;  DB 17;  Length 70;
  Best Local Similarity   100.0%;  Pred. No. 3.1e-16;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
          |||||||||||||||||||||||||||||||
Db     20 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 50


RESULT 2
AAO15165
ID   AAO15165 standard; peptide; 116 AA.
XX
AC   AAO15165;
XX
DT   02-SEP-2002  (first entry)
XX
DE   Clostridial neurotoxin protease substrate peptide 4.
XX
KW   Clostridial neurotoxin substrate; botulinum neurotoxin substrate; FRET;
KW   fluorescence resonant energy transfer assay; quenched-signal;
KW   clostridial neurotoxin detection; food.
XX
OS   Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "S-fluoresceinyl-cysteine"
FT   Cleavage-site   89..90
FT                   /note= "The peptide is cleaved between these two
FT                   residues by type E Clostridium botulinum neurotoxin"
FT   Cleavage-site   106..107
FT                   /note= "The peptide is cleaved between these two
FT                   residues by type A Clostridium botulinum neurotoxin"
XX
PN   WO200225284-A2.
XX
PD   28-MAR-2002.
XX
PF   25-SEP-2001; 2001WO-US30188.
XX
PR   25-SEP-2000; 2000US-235050P.
XX
PA   (USME-) US MEDICAL RES INST INFECTIOUS DISEASES.
XX
PI   Schmidt JJ,  Stafford RG;
XX
DR   WPI; 2002-499829/53.
XX
PT   Substrate useful in e.g. an assay for the protease activity of
PT   clostridial neurotoxin, comprises modified peptide or protein -
XX
PS   Claim 22; Page 16; 48pp; English.
XX
CC   The invention comprises clostridial neurotoxin substrate peptides which
CC   can serve as fluorescence resonant energy transfer assay (FRET) or
CC   quenched-signal substrates in assays for the proteolytic activities of
CC   clostridial neurotoxins. The invention further comprises Clostridium
CC   botulinum neurotoxin substrate peptides that can serve as immobilised
CC   substrates (i.e. bound to a solid phase) in assays for the proteolytic
CC   activities of clostridial neurotoxins. The clostridial (including the
CC   Clostridium botulinum) neurotoxin substrate peptides are useful for
CC   detecting the presence of clostridial neurotoxins in a sample (e.g. food
CC   or an environmental sample). The present amino acid sequence represents a
CC   clostridial neurotoxin substrate peptide of the invention.
XX
SQ   Sequence   116 AA;

  Query Match             100.0%;  Score 158;  DB 23;  Length 116;
  Best Local Similarity   100.0%;  Pred. No. 5.6e-16;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
          |||||||||||||||||||||||||||||||
Db     65 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 95


RESULT 3
AAO15166
ID   AAO15166 standard; peptide; 116 AA.
XX
AC   AAO15166;
XX
DT   02-SEP-2002  (first entry)
XX
DE   Clostridial neurotoxin protease substrate peptide 5.
XX
KW   Clostridial neurotoxin substrate; botulinum neurotoxin substrate; FRET;
KW   fluorescence resonant energy transfer assay; quenched-signal;
KW   clostridial neurotoxin detection; food.
XX
OS   Unidentified.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   1
FT                   /note= "S-fluoresceinyl-cysteine"
FT   Cleavage-site   89..90
FT                   /note= "The peptide is cleaved between these two
FT                   residues by type E Clostridium botulinum neurotoxin"
XX
PN   WO200225284-A2.
XX
PD   28-MAR-2002.
XX
PF   25-SEP-2001; 2001WO-US30188.
XX
PR   25-SEP-2000; 2000US-235050P.
XX
PA   (USME-) US MEDICAL RES INST INFECTIOUS DISEASES.
XX
PI   Schmidt JJ,  Stafford RG;
XX
DR   WPI; 2002-499829/53.
XX
PT   Substrate useful in e.g. an assay for the protease activity of
PT   clostridial neurotoxin, comprises modified peptide or protein -
XX
PS   Claim 28; Page 17; 48pp; English.
XX
CC   The invention comprises clostridial neurotoxin substrate peptides which
CC   can serve as fluorescence resonant energy transfer assay (FRET) or
CC   quenched-signal substrates in assays for the proteolytic activities of
CC   clostridial neurotoxins. The invention further comprises Clostridium
CC   botulinum neurotoxin substrate peptides that can serve as immobilised
CC   substrates (i.e. bound to a solid phase) in assays for the proteolytic
CC   activities of clostridial neurotoxins. The clostridial (including the
CC   Clostridium botulinum) neurotoxin substrate peptides are useful for
CC   detecting the presence of clostridial neurotoxins in a sample (e.g. food
CC   or an environmental sample). The present amino acid sequence represents a
CC   clostridial neurotoxin substrate peptide of the invention.
XX
SQ   Sequence   116 AA;
```

```
  Query Match             100.0%;  Score 158;  DB 23;  Length 116;
  Best Local Similarity   100.0%;  Pred. No. 5.6e-16;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
           |||||||||||||||||||||||||||||||
Db      65 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 95


RESULT 4
AAU00255
ID   AAU00255 standard; Protein; 198 AA.
XX
AC   AAU00255;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, C-terminal deletion 1-198.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, C-terminal deletion 1-198, used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   198 AA;

  Query Match             100.0%;  Score 158;  DB 22;  Length 198;
  Best Local Similarity   100.0%;  Pred. No. 1e-15;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
           |||||||||||||||||||||||||||||||
Db     156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186


RESULT 5
AAU00263
ID   AAU00263 standard; Protein; 199 AA.
XX
AC   AAU00263;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant 1-199(R198T).
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant 1-199(R198T), used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
```

CC polynucleotide encoding either of these SNARE polypeptides are useful in
CC the manufacture of medicament for the treatment of a patient in need of
CC inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis. The method of treatment is
CC relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
CC Note: The present sequence is not shown in the specification but is
CC derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ Sequence 199 AA;

Query Match 100.0%; Score 158; DB 22; Length 199;
Best Local Similarity 100.0%; Pred. No. 1e-15;
Matches 31; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
||||||||||||||||||||||||||||||
Db 156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186

RESULT 6
AAU00264
ID AAU00264 standard; Protein; 200 AA.
XX
AC AAU00264;
XX
DT 12-SEP-2001 (first entry)
XX
DE Synaptosomal-associated protein, SNAP25, mutant 1-200(R198T).
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; mouse; mutant; mutein;
KW N-ethylmaleimide-sensitive fusion protein;
KW soluble NSF-attachment protein receptor.
XX
OS Mus sp.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 198
FT /note= "Wild-type Arg substituted by Thr"
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Example 1; Page - ; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25, mutant 1-200(R198T), used in a new
CC method of treating a patient suffering from poisoning or at risk of
CC poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC to a cell of the patient, where the SNARE is resistant to proteolysis by
CC the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC treating a patient in need of inhibition of SNARE-dependent exocytosis
CC from a cell capable of performing SNARE-dependent exocytosis, comprises
CC supplying a fragment, variant, fusion or derivative of a SNARE or an
CC inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC useful in the manufacture of a medicament for the treatment of a patient
CC suffering from poisoning or at risk of poisoning by clostridial toxin,
CC e.g. from botulism or tetanus. The fragment, variant, fusion or
CC derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC polynucleotide encoding either of these SNARE polypeptides are useful in
CC the manufacture of medicament for the treatment of a patient in need of
CC inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis. The method of treatment is
CC relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
CC Note: The present sequence is not shown in the specification but is
CC derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ Sequence 200 AA;

Query Match 100.0%; Score 158; DB 22; Length 200;
Best Local Similarity 100.0%; Pred. No. 1.1e-15;
Matches 31; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
||||||||||||||||||||||||||||||
Db 156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186

RESULT 7
AAU02637
ID AAU02637 standard; Protein; 201 AA.
XX
AC AAU02637;
XX
DT 12-SEP-2001 (first entry)
XX
DE Synaptosomal-associated protein, SNAP25, mutant 1-201(R198T).
XX
KW SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW synaptosomal-associated protein; mouse; mutant; mutein;
KW N-ethylmaleimide-sensitive fusion protein;
KW soluble NSF-attachment protein receptor.
XX
OS Mus sp.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 198
FT /note= "Wild-type Arg substituted by Thr"
XX
PN WO200118038-A2.
XX
PD 15-MAR-2001.
XX
PF 18-AUG-2000; 2000WO-GB03196.
XX
PR 20-AUG-1999; 99US-0149993.
XX
PA (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Example 1; Page - ; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25, mutant 1-201(R198T), used in a new
CC method of treating a patient suffering from poisoning or at risk of

```
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   201 AA;

  Query Match           100.0%;  Score 158;  DB 22;  Length 201;
  Best Local Similarity  100.0%;  Pred. No. 1.1e-15;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
          |||||||||||||||||||||||||||||||
Db    156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186


RESULT 8
AAU00265
ID   AAU00265 standard; Protein; 202 AA.
XX
AC   AAU00265;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant 1-202(R198T).
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Example 1; Page - ; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25, mutant 1-202(R198T), used in a new
CC   method of treating a patient suffering from poisoning or at risk of
CC   poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC   (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC   to a cell of the patient, where the SNARE is resistant to proteolysis by
CC   the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC   toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC   treating a patient in need of inhibition of SNARE-dependent exocytosis
CC   from a cell capable of performing SNARE-dependent exocytosis, comprises
CC   supplying a fragment, variant, fusion or derivative of a SNARE or an
CC   inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC   inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC   useful in the manufacture of a medicament for the treatment of a patient
CC   suffering from poisoning or at risk of poisoning by clostridial toxin,
CC   e.g. from botulism or tetanus. The fragment, variant, fusion or
CC   derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC   polynucleotide encoding either of these SNARE polypeptides are useful in
CC   the manufacture of medicament for the treatment of a patient in need of
CC   inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis. The method of treatment is
CC   relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
CC   Note: The present sequence is not shown in the specification but is
CC   derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ   Sequence   202 AA;

  Query Match           100.0%;  Score 158;  DB 22;  Length 202;
  Best Local Similarity  100.0%;  Pred. No. 1.1e-15;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy      1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
          |||||||||||||||||||||||||||||||
Db    156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186


RESULT 9
AAU02636
ID   AAU02636 standard; Protein; 203 AA.
XX
AC   AAU02636;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25, mutant 1-203(R198T).
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mouse; mutant; mutein;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
OS   Synthetic.
XX
FH   Key             Location/Qualifiers
FT   Misc-difference 198
FT                   /note= "Wild-type Arg substituted by Thr"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
```

XX
PI Dolly JO, O'Sullivan GA, Mohammed N, Foran PG;
XX
DR WPI; 2001-226739/23.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Example 1; Page - ; 131pp; English.
XX
CC The sequence represents the amino acid sequence of synaptosomal-
CC associated protein, SNAP25, mutant 1-203(R198T), used in a new
CC method of treating a patient suffering from poisoning or at risk of
CC poisoning by a clostridial toxin, comprising supplying a SNARE (soluble
CC (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor)
CC to a cell of the patient, where the SNARE is resistant to proteolysis by
CC the toxin (toxin-resistant SNARE) and/or is capable of inhibiting the
CC toxin (toxin-inhibitory SNARE). The protein can be used in a method of
CC treating a patient in need of inhibition of SNARE-dependent exocytosis
CC from a cell capable of performing SNARE-dependent exocytosis, comprises
CC supplying a fragment, variant, fusion or derivative of a SNARE or an
CC inhibitory SNARE to the cell of the patient. The toxin resistant or toxin
CC inhibitory SNARE or a recombinant polynucleotide encoding the SNARE is
CC useful in the manufacture of a medicament for the treatment of a patient
CC suffering from poisoning or at risk of poisoning by clostridial toxin,
CC e.g. from botulism or tetanus. The fragment, variant, fusion or
CC derivative of a SNARE or of an inhibitory SNARE, or a recombinant
CC polynucleotide encoding either of these SNARE polypeptides are useful in
CC the manufacture of medicament for the treatment of a patient in need of
CC inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis. The method of treatment is
CC relatively fast, thus alleviating the symptoms when most severe and
CC taking the patient out of critical state.
CC Note: The present sequence is not shown in the specification but is
CC derived from the mouse SNAP-25 sequence given in figure 8 (see AAU00246).
XX
SQ Sequence 203 AA;

Query Match 100.0%; Score 158; DB 22; Length 203;
Best Local Similarity 100.0%; Pred. No. 1.1e-15;
Matches 31; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
||||||||||||||||||||||||||||||
Db 156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186

RESULT 10
AAW30103
ID AAW30103 standard; peptide; 206 AA.
XX
AC AAW30103;
XX
DT 06-APR-1998 (first entry)
XX
DE Synaptosomal associated protein.
XX
KW Neurotransmitter secretion; inhibitor; neuronal cell; synaptic vesicle;
KW excitation-secretory uncoupling peptide; catecholamine secretion;
KW bovine chromaffin cell; Clostridium toxin; muscle spasticity reduction;
KW synaptosomal associated protein; SNAP-25.
XX
OS Homo sapiens.
XX
PN WO9734620-A1.
XX
PD 25-SEP-1997.
XX
PF 18-MAR-1997; 97WO-US04393.
XX
PR 18-MAR-1996; 96US-0013599.
XX
PA (REGC) UNIV CALIFORNIA.
XX
PI Montal M;
XX
DR WPI; 1997-479986/44.
XX
PT Excitation-secretory uncoupling peptide(s) for inhibiting
PT neuro:transmitter release - used particularly for treating muscle
PT spasticity, and for delivering drugs specifically to neural cells
XX
PS Disclosure; Page 27-28; 61pp; English.
XX
CC This sequence represents the human 25 kD synaptosomal associated protein
CC (SNAP-25), which is an inhibitory agent of the invention. The agents of
CC the invention inhibit secretion of neurotransmitter from neuronal cells
CC and is an excitation-secretory uncoupling peptide (I) of at least 20
CC amino acids (aa) all of which correspond substantially to any one of
CC AAW30097-W30102, or more generally any (I) that inhibits 50% of
CC catecholamine secretion from bovine chromaffin cells at a concentration
CC of 10 microM, especially 0.25 microM, or less. (I) are used, as a
CC replacement for Clostridium toxin, to inhibit release of
CC neurotransmitters from synaptic vesicles, specifically for reducing
CC muscle spasticity. Also (I) may be labelled to allow in vivo imaging of
CC intracellular distribution of (I). Compounds for delivering the drug to
CC neural cells provide targeted drug delivery, e.g. of substance P to
CC brain tumours for induction of apoptosis. Unlike the neurotoxins, (I) are
CC not toxic or immunogenic and are more readily available. Their
CC therapeutic effect lasts for several days or weeks, so lower doses or
CC less frequent treatments are required.
XX
SQ Sequence 206 AA;

Query Match 100.0%; Score 158; DB 18; Length 206;
Best Local Similarity 100.0%; Pred. No. 1.1e-15;
Matches 31; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
||||||||||||||||||||||||||||||
Db 156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186

RESULT 11
AAW79198
ID AAW79198 standard; Protein; 206 AA.
XX
AC AAW79198;
XX
DT 25-NOV-1998 (first entry)
XX
DE Mouse SNAP-25 polypeptide.
XX
KW Hrs-2 polypeptide; ATP-preferring nucleotidase; SNAP-25; vesicle docking;
KW calcium-regulated secretion; secretory vesicle; secretory process; brain;
KW neurotransmitter release; presynaptic membrane; CNS disorder; depression;
KW Parkinson's disease; endocrine system; hormonal imbalance; cell division;
KW thought disorder; schizophrenia; degenerative disorder; anaesthesia; rat;
KW immune system; antigen processing; immunomodulator; viral processing;
KW central nervous system; vesicular release; affective disorder; human;
KW anti-tumour application; membrane trafficking regulation; mouse.
XX
OS Mus sp.
XX
PN WO9838210-A2.
XX
PD 03-SEP-1998.
XX
PF 26-FEB-1998; 98WO-US03789.
XX
PR 26-FEB-1997; 97US-0039159.
XX
PA (STRD) UNIV LELAND STANFORD JUNIOR.
XX
PI Bean AJ, Scheller RH;

```
XX
DR   WPI; 1998-481140/41.
DR   N-PSDB; AAV57558.
XX
PT   New isolated Hrs-2 nucleotidase - used in assays to identify
PT   compounds capable of modulating calcium-regulatory secretion of
PT   secretory vesicles, such as in neurotransmitter release
XX
PS   Claim 16; Pages 42-44; 55pp; English.
XX
CC   This represents a mouse SNAP-25 polypeptide, a component of the protein
CC   polypeptides thought to underlie vesicle docking and fusion. The
CC   invention provides rat and human Hrs-2 polypeptides which are ATP-
CC   preferring nucleotidase that associate with SNAP-25. For identifying a
CC   compound capable of modulating calcium-regulated secretion of secretory
CC   vesicles, a SNAP-25 polypeptide can be contacted with a Hrs-2
CC   polypeptide, in the presence and absence of a test compound. The effect
CC   of the test compound on the extent of binding between the SNAP-25 and
CC   Hrs-2 polypeptides are measured and a compound is identified as effective
CC   if its measured effect on the extent of binding is above a threshold
CC   level. The products can be used for identifying drugs capable of
CC   affecting secretory processes, such as neurotransmitter release at the
CC   active zones of presynaptic membranes. Such drugs can be used for
CC   treating disorders or conditions of the central nervous system by
CC   selectively enhancing or inhibiting vesicular release in specific areas
CC   of the brain, including affective disorders (e.g. depression), disorders
CC   of thought (e.g. schizophrenia) and degenerative disorders ( Parkinson's
CC   disease), as well as applications such as anaesthesia. The drugs can
CC   also be used therapeutically in other systems such as the endocrine
CC   system for treatment of hormonal imbalances, the immune system for
CC   intervention in antigen processing, secreted immunomodulators, and viral
CC   processing, as well as anti-tumour applications, such as regulation of
CC   membrane trafficking during rapid cell division.
XX
SQ   Sequence   206 AA;

  Query Match             100.0%;  Score 158;  DB 19;  Length 206;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-15;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
           |||||||||||||||||||||||||||||||
Db     156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186


RESULT 12
AAW43426
ID   AAW43426 standard; Protein; 206 AA.
XX
AC   AAW43426;
XX
DT   27-APR-1998  (first entry)
XX
DE   Mouse synaptosomal-associated protein-25.
XX
KW   Binding domain; mouse; syntaxin; synaptosomal-associated protein; CNS;
KW   neurotransmitter; presynaptic membrane; central nervous system; tumour;
KW   neurodegenerative disease; hormonal disorder; immunological disorder.
XX
OS   Mus sp.
XX
PN   US5693476-A.
XX
PD   02-DEC-1997.
XX
PF   24-FEB-1995;   95US-0393985.
XX
PR   24-FEB-1995;   95US-0393985.
XX
PA   (STRD ) UNIV LELAND STANFORD JUNIOR.
XX
PI   Scheller RH;
XX
DR   WPI; 1998-031743/03.
DR   N-PSDB; AAV01554.
XX
PT   Screening assay for modulators of syntaxin binding - using peptide
PT   comprising binding site of syntaxin, for identifying drugs useful
PT   for treating CNS disorders, neuro-degenerative diseases, etc
XX
PS   Disclosure; Column 67-72; 57pp; English.
XX
CC   This amino acid sequence represents the mouse synaptosomal-associated
CC   protein of 25 kD (SNAP-25).  The invention relates to a method for
CC   identifying a compound capable of affecting the binding of a
CC   syntaxin-binding protein (SBP), e.g. SNAP-25, alpha-SNAP, n-sec1 or VAMP,
CC   to syntaxin.  The method comprises measuring the effect of the test
CC   compound on the extent of binding between the SBP and the SBP-binding
CC   site on syntaxin.  The method can be used for identifying drugs capable
CC   of inhibiting or stimulating neurotransmitter release at the active zones
CC   of presynaptic membranes, which may be useful for treating CNS disorders,
CC   affective or psychotic disorders, neurodegenerative diseases, hormonal or
CC   immunological disorders or tumours.
XX
SQ   Sequence   206 AA;

  Query Match             100.0%;  Score 158;  DB 19;  Length 206;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-15;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
           |||||||||||||||||||||||||||||||
Db     156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186


RESULT 13
AAU00246
ID   AAU00246 standard; Protein; 206 AA.
XX
AC   AAU00246;
XX
DT   12-SEP-2001  (first entry)
XX
DE   Synaptosomal-associated protein, SNAP25.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; mutagenic; PCR primer; mouse;
KW   N-ethylmaleimide-sensitive fusion protein;
KW   soluble NSF-attachment protein receptor.
XX
OS   Mus sp.
XX
XX
FH   Key             Location/Qualifiers
FT   Cleavage-site   180..181
FT                   /note= "Peptide bond susceptible to cleavage by
FT                         clostridial neurotoxin"
FT   Cleavage-site   197..198
FT                   /note= "Peptide bonds susceptible to cleavage by
FT                         clostridial neurotoxin"
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
XX
```

```
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Disclosure; Fig 8; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of synaptosomal-
CC   associated protein, SNAP25. The sequence was used to
CC   create SNAP-25 double/single point mutants and C-terminal deletion
CC   mutants used in a new method of treating a patient suffering from
CC   poisoning or at risk of poisoning by a clostridial toxin, comprising
CC   supplying a SNARE (soluble (N-ethylmaleimide-sensitive fusion protein)-
CC   attachment protein receptor) to a cell of the patient, where the SNARE is
CC   resistant to proteolysis by the toxin (toxin-resistant SNARE) and/or is
CC   capable of inhibiting the toxin (toxin-inhibitory SNARE). The protein can
CC   be used in a method of treating a patient in need of inhibition of SNARE-
CC   dependent exocytosis from a cell capable of performing SNARE-dependent
CC   exocytosis, comprises supplying a fragment, variant, fusion or derivative
CC   of a SNARE or an inhibitory SNARE to the cell of the patient. The toxin
CC   resistant or toxin inhibitory SNARE or a recombinant polynucleotide
CC   encoding the SNARE is useful in the manufacture of a medicament for the
CC   treatment of a patient suffering from poisoning or at risk of poisoning
CC   by clostridial toxin, e.g. from botulism or tetanus. The fragment,
CC   variant, fusion or derivative of a SNARE or of an inhibitory SNARE, or a
CC   recombinant polynucleotide encoding either of these SNARE polypeptides
CC   are useful in the manufacture of medicament for the treatment of a
CC   patient in need of inhibition of SNARE-dependent exocytosis from a cell
CC   capable of performing SNARE-dependent exocytosis. The method of treatment
CC   is relatively fast, thus alleviating the symptoms when most severe and
CC   taking the patient out of critical state.
XX
SQ   Sequence   206 AA;

  Query Match             100.0%;  Score 158;  DB 22;  Length 206;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-15;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
           |||||||||||||||||||||||||||||||
Db     156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186


RESULT 14
AAU00252
ID   AAU00252 standard; Protein; 206 AA.
XX
AC   AAU00252;
XX
DT   12-SEP-2001  (first entry)
XX
DE   SNARE homologue, synaptosomal-associated protein, hSNAP25a.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; hSNAP25a; human;
KW   N-ethylmaleimide-sensitive fusion;
KW   soluble NSF-attachment protein receptor.
XX
OS   Homo sapiens.
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
DR   N-PSDB; AAS00369.
XX
PT   Treating a patient suffering from poisoning or at risk of poisoning by
PT   a clostridial toxin, e.g. botulism, comprises administering a
PT   toxin-resistant or toxin-inhibitory SNARE -
XX
PS   Disclosure; Fig 8; 131pp; English.
XX
CC   The sequence represents the amino acid sequence of SNARE homologue,
CC   synaptosomal-associated membrane protein, hSNAP25a, used during analysis
CC   of SNAP-25. SNAP-25 mutants were used in a new method of treating a
CC   patient suffering from poisoning or at risk of poisoning by a clostridial
CC   toxin, comprising supplying a SNARE (soluble (N-ethylmaleimide-sensitive
CC   fusion protein)-attachment protein receptor) to a cell of the patient,
CC   where the SNARE is resistant to proteolysis by the toxin (toxin-resistant
CC   SNARE) and/or is capable of inhibiting the toxin (toxin-inhibitory
CC   SNARE). The protein can be used in a method of treating a patient in need
CC   of inhibition of SNARE-dependent exocytosis from a cell capable of
CC   performing SNARE-dependent exocytosis, comprises supplying a fragment,
CC   variant, fusion or derivative of a SNARE or an inhibitory SNARE to the
CC   cell of the patient. The toxin resistant or toxin inhibitory SNARE or a
CC   recombinant polynucleotide encoding the SNARE is useful in the
CC   manufacture of a medicament for the treatment of a patient suffering from
CC   poisoning or at risk of poisoning by clostridial toxin, e.g. from
CC   botulism or tetanus. The fragment, variant, fusion or derivative of a
CC   SNARE or of an inhibitory SNARE, or a recombinant polynucleotide encoding
CC   either of these SNARE polypeptides are useful in the manufacture of
CC   medicament for the treatment of a patient in need of inhibition of SNARE-
CC   dependent exocytosis from a cell capable of performing SNARE-dependent
CC   exocytosis. The method of treatment is relatively fast, thus
CC   alleviating the symptoms when most severe and taking the patient out of
CC   critical state.
XX
SQ   Sequence   206 AA;

  Query Match             100.0%;  Score 158;  DB 22;  Length 206;
  Best Local Similarity   100.0%;  Pred. No. 1.1e-15;
  Matches   31;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
           |||||||||||||||||||||||||||||||
Db     156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186


RESULT 15
AAU00253
ID   AAU00253 standard; Protein; 206 AA.
XX
AC   AAU00253;
XX
DT   12-SEP-2001  (first entry)
XX
DE   SNARE homologue, synaptosomal-associated protein, hSNAP25b.
XX
KW   SNAP-25; poisoning; clostridial toxin; SNARE; toxin-resistant SNARE;
KW   toxin-inhibitory SNARE; botulism; tetanus; SNARE-dependent exocytosis;
KW   synaptosomal-associated protein; hSNAP25b; human.
XX
OS   Homo sapiens.
XX
PN   WO200118038-A2.
XX
PD   15-MAR-2001.
XX
PF   18-AUG-2000; 2000WO-GB03196.
XX
PR   20-AUG-1999;   99US-0149993.
XX
PA   (IMCO-) IMPERIAL COLLEGE INNOVATIONS LTD.
XX
PI   Dolly JO,  O'Sullivan GA,  Mohammed N,  Foran PG;
XX
DR   WPI; 2001-226739/23.
```

DR N-PSDB; AAS00370.
XX
PT Treating a patient suffering from poisoning or at risk of poisoning by
PT a clostridial toxin, e.g. botulism, comprises administering a
PT toxin-resistant or toxin-inhibitory SNARE -
XX
PS Disclosure; Fig 8; 130pp; English.
XX
CC The sequence represents the amino acid sequence of SNARE homologue,
CC synaptosomal-associated membrane protein, hSNAP25b, used during analysis
CC of SNAP-25. SNAP-25 mutants were used in a new method of treating a
CC patient suffering from poisoning or at risk of poisoning by a clostridial
CC toxin, comprising supplying a SNARE (soluble (N-ethylmaleimide-sensitive
CC fusion protein)-attachment protein receptor) to a cell of the patient,
CC where the SNARE is resistant to proteolysis by the toxin (toxin-resistant
CC SNARE) and/or is capable of inhibiting the toxin (toxin-inhibitory
CC SNARE). The protein can be used in a method of treating a patient in need
CC of inhibition of SNARE-dependent exocytosis from a cell capable of
CC performing SNARE-dependent exocytosis, comprises supplying a fragment,
CC variant, fusion or derivative of a SNARE or an inhibitory SNARE to the
CC cell of the patient. The toxin resistant or toxin inhibitory SNARE or a
CC recombinant polynucleotide encoding the SNARE is useful in the
CC manufacture of a medicament for the treatment of a patient suffering from
CC poisoning or at risk of poisoning by clostridial toxin, e.g. from
CC botulism or tetanus. The fragment, variant, fusion or derivative of a
CC SNARE or of an inhibitory SNARE, or a recombinant polynucleotide encoding
CC either of these SNARE polypeptides are useful in the manufacture of
CC medicament for the treatment of a patient in need of inhibition of SNARE-
CC dependent exocytosis from a cell capable of performing SNARE-dependent
CC exocytosis. The method of treatment is relatively fast, thus
CC alleviating the symptoms when most severe and taking the patient out of
CC critical state.
XX
SQ Sequence 206 AA;

Query Match 100.0%; Score 158; DB 22; Length 206;
Best Local Similarity 100.0%; Pred. No. 1.1e-15;
Matches 31; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy       1 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 31
           |||||||||||||||||||||||||||||||
Db     156 IIGNLRHMALDMGNEIDTQNRQIDRIMEKAD 186
```

Search completed: November 19, 2002, 17:39:13
Job time : 40.6875 secs

```
=> file reg
FILE 'REGISTRY' ENTERED AT 16:02:48 ON 03 DEC 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    2 DEC 2002  HIGHEST RN 474876-19-2
DICTIONARY FILE UPDATES:   2 DEC 2002  HIGHEST RN 474876-19-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d que l1
L1           78 SEA FILE=REGISTRY ABB=ON  PLU=ON  EANQRA|ANQRAT|NQRATK/SQSP


=> file caplus; d que l7
FILE 'CAPLUS' ENTERED AT 16:08:29 ON 03 DEC 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 3 Dec 2002  VOL 137 ISS 23
FILE LAST UPDATED: 2 Dec 2002  (20021202/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.


L1           78 SEA FILE=REGISTRY ABB=ON  PLU=ON  EANQRA|ANQRAT|NQRATK/SQSP
L2           44 SEA FILE=CAPLUS ABB=ON  PLU=ON  L1
L3         4704 SEA FILE=CAPLUS ABB=ON  PLU=ON  BOTUL?
L4           20 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 AND L3
```

THIS PAGE BLANK (USPTO)

```
L5          1235 SEA FILE=CAPLUS ABB=ON  PLU=ON  BONT?
L6             9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 AND L5
L7            20 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 OR L6


=> d ibib ab hitrn l7 1-20

L7   ANSWER 1 OF 20  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:869489  CAPLUS
TITLE:                    Recombinant light chains of botulinum
                          neurotoxins and light chain fusion proteins for use in
                          research and clinical therapy
INVENTOR(S):              Smith, Leonard; Jensen, Melody
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 99 pp., Cont.-in-part of U.S.
                          Ser. No. 910,186.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     US 2002168727      A1   20021114       US 2001-11588     20011106
PRIORITY APPLN. INFO.:                   US 1993-123975    B1 19930921
                                         US 1999-133865P   P  19990512
                                         US 1999-133866P   P  19990512
                                         US 1999-133867P   P  19990512
                                         US 1999-133868P   P  19990512
                                         US 1999-133869P   P  19990512
                                         US 1999-133873P   P  19990512
                                         US 2000-611419    A1 20000706
                                         US 2000-246774P   P  20001106
                                         US 2001-910186    A2 20010720
                                         US 2001-311966P   P  20010809
```

AB **Botulinum** neurotoxins, the most potent of all toxins, induce lethal neuromuscular paralysis by inhibiting exocytosis at the neuromuscular junction. The light chains (LC) of these dichain neurotoxins are a new class of zinc-endopeptidases that specifically cleave the synaptosomal proteins, SNAP-25, VAMP, or syntaxin at discrete sites. The present invention relates to the construction, expression, purifn., and use of synthetic or recombinant **botulinum** neutoroxin genes. For example, a synthetic gene for the LC of the **botulinum** neurotoxin serotype A (**BoNT**/A) was constructed and overexpressed in Escherichia coli.The gene product was purified from inclusion bodies. The methods of the invention can provide 1.1 g of the LC per L of culture. The LC product was stable in soln. at 4.degree. C. for at least 6 mo. This rBoNT/A LC was proteolytically active, specifically cleaving the Glu-Arg bond in a 17-residue synthetic peptide of SNAP-25, the reported cleavage site of **BoNT**/A. Its calcd. catalytic efficiency k"ub.degree.cat sub.degree./K"ub.degree.m sub.degree.was higher than that reported for the native **BoNT**/A dichain. Treating the rBoNT/A LC with mercuric compds. completely abolished its activity, most probably by modifying the cysteine-164 residue located in the vicinity of the active site. About 70% activity of the LC was restored by adding Zn"up.degree.2+"up.degree. to a Zn"up.degree.2+"up.degree. -free apo-LC prepn. The LC was nontoxic to mice and failed to elicit neutralizing epitope(s) when the animals were vaccinated with this protein. In addn., injecting rBoNT/A LC into sea urchin eggs inhibited exocytosis-dependent plasma membrane resealing.

IT INDEXING IN PROGRESS
IT **216568-37-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide sybstrate; recombinant light chains of **botulinum** neurotoxins and light chain fusion proteins for use in research and clin. therapy)
IT **188592-00-9**
RL: PRP (Properties)
(unclaimed sequence; recombinant light chains of **botulinum** neurotoxins and light chain fusion proteins for use in research and clin. therapy)

L7 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:595499 CAPLUS
DOCUMENT NUMBER: 137:145554
TITLE: Methods of administering **botulinum** toxin
INVENTOR(S): Walker, Patricia S.
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U. S. Ser. No. 730,237.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002107199	A1	20020808	US 2002-51952	20020117
US 2002086036	A1	20020704	US 2000-730237	20001205

PRIORITY APPLN. INFO.: US 2000-730237 A2 20001205
AB Methods for treating conditions in an animal or human subject are disclosed. The conditions may be pain, skeletal muscle conditions, smooth muscle conditions, glandular conditions and cosmetic conditions. The methods comprise the step of administering a Clostridium neurotoxin component or Clostridium neurotoxin component-encoding DNA to the subject using a needleless syringe.
IT **439904-18-4**
RL: PRP (Properties)
(unclaimed sequence; administration of **botulinum** toxin)

L7 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:505236 CAPLUS
DOCUMENT NUMBER: 137:83622
TITLE: Methods for treating hyperhidrosis
INVENTOR(S): Walker, Patricia S.
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002086036	A1	20020704	US 2000-730237	20001205
US 2002107199	A1	20020808	US 2002-51952	20020117

PRIORITY APPLN. INFO.: US 2000-730237 A2 20001205
AB Methods for treating hyperhidrosis is disclosed herein. In one

embodiment, the method includes a step of administering a neurotoxin to a skin area to alleviate excessive sweating. In another embodiment, the method employs a needleless injector to affect the administration of a neurotoxin, for example **botulinum** toxin type A.

IT **439904-18-4**
RL: PRP (Properties)
(unclaimed sequence; methods for treating hyperhidrosis)

L7 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:353597 CAPLUS
DOCUMENT NUMBER: 136:365216
TITLE: Recombinant light chains of **botulinum** neurotoxins and light chain fusion proteins for use in research and clinical therapy
INVENTOR(S): Smith, Leonard A.; Jensen, Melody
PATENT ASSIGNEE(S): United States Army Medical Research and Material Command, USA
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036758	A2	20020510	WO 2001-US47230	20011106
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002028887	A5	20020515	AU 2002-28887	20011106

PRIORITY APPLN. INFO.:
US 2000-246774P P 20001106
US 2001-910186 A 20010720
US 2001-311966P P 20010809
WO 2001-US47230 W 20011106

AB **Botulinum** neurotoxins, the most potent of all toxins, induce lethal neuromuscular paralysis by inhibiting exocytosis at the neuromuscular junction. The light chains (LC) of these dichain neurotoxins are a new class of zinc-endopeptidases that specifically cleave the synaptosomal proteins, SNAP-25, VAMP, or syntaxin at discrete sites. The present invention relates to the construction, expression, purifn., and use of synthetic or recombinant **botulinum** neurotoxin genes. For example, a synthetic gene for the LC of the **botulinum** neurotoxin serotype A (**BoNT**/A) was constructed and overexpressed in Escherichia coli. The gene product was purified from inclusion bodies. The methods of the invention can provide 1.1 g of the LC per L of culture. The LC product was stable in soln. at 4.degree. for at least 6 mo. This rBoNT/A LC was proteolytically active, specifically cleaving the Glu-Arg bond in a 17-residue synthetic peptide of SNAP-25, the reported cleavage site of **BoNT**/A. Its calcd. catalytic efficiency kcat/Km was higher than that reported for the native **BoNT**/A dichain. Treating the rBoNT/A LC with mercuric compds. completely abolished its activity, most probably by modifying the cysteine-164 residue located in the vicinity of the active site. About 70% activity of the LC was restored by adding Zn2+-free, apo-LC prepn.

The LC was nontoxic to mice and failed to elicit neutralizing epitope(s) when the animals were vaccinated with this protein. In addn., injecting rBoNT/A LC into sea urchin eggs inhibited exocytosis-dependent plasma membrane resealing.

IT **216568-37-5**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide sybstrate; recombinant light chains of **botulinum** neurotoxins and light chain fusion proteins for use in research and clin. therapy)

IT **188592-00-9**
RL: PRP (Properties)
(unclaimed sequence; recombinant light chains of **botulinum** neurotoxins and light chain fusion proteins for use in research and clin. therapy)

L7 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:286211 CAPLUS
DOCUMENT NUMBER: 136:290338
TITLE: Peptides that mimic the carboxy-terminal domain of SNAP-25 block acetylcholine release at an Aplysia synapse. [Erratum to document cited in CA132:304502]
AUTHOR(S): Apland, J. P.; Biser, J. A.; Adler, M.; Ferrer-Montiel, A. V.; Montal, M.; Canaves, J. M.; Filbert, M. G.
CORPORATE SOURCE: Neurotoxicology Branch, US Army Medical Research Institue of Chemical Defense, Aberdeen Proving Ground, MD, 21010-5400, USA
SOURCE: Journal of Applied Toxicology (2000), 20(6), 499
CODEN: JJATDK; ISSN: 0260-437X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The cor. author information is given.
IT **169265-36-5 196928-77-5**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(peptides mimicking carboxy-terminal domain of SNAP-25 block acetylcholine release at Aplysia synapse (Erratum))

L7 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:241093 CAPLUS
DOCUMENT NUMBER: 136:274685
TITLE: Fluorescent substrates and high throughput assays for proteotytic activities of clostridial neurotoxins
INVENTOR(S): Schmidt, James J.; Stafford, Robert G.
PATENT ASSIGNEE(S): U.S. Medical Research Institute of Infectious Diseases, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002025284	A2	20020328	WO 2001-US30188	20010925

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-235050P P 20000925

AB In this application is described substrates for high-throughput assays of clostridial neurotoxin proteolytic activities. Two types of substrates are described: (1) modified peptides or proteins that can serve as FRET substrates and (2) modified peptides or proteins that can serve as immobilized substrates. In both types a fluorescent mol. is present in the substrate, eliminating the requirement for the addn. of a fluorigenic reagent. The assays described can be readily adapted for use in automated or robotic systems.

IT **405665-86-3 406458-86-4**
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)
(fluorescent substrates and high throughput assays for proteotytic activities of clostridial neurotoxins)

L7 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:618890 CAPLUS

DOCUMENT NUMBER: 136:50089

TITLE: High-throughput assays for **botulinum** neurotoxin proteolytic activity: Serotypes A, B, D, and F

AUTHOR(S): Schmidt, James J.; Stafford, Robert G.; Millard, Charles B.

CORPORATE SOURCE: Department of Cell Biology and Biochemistry, Toxicology and Aerobiology Division, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD, 21702-5011, USA

SOURCE: Analytical Biochemistry (2001), 296(1), 130-137
CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Botulinum** neurotoxins (**BoNT**) are zinc metalloproteases that cleave and inactivate cellular proteins essential for neurotransmitter release. Because the paralytic effect of **BoNT** is a consequence of its enzymic activity, selective inhibitors may be useful as drugs or as tools for further research. To expedite inhibitor discovery, the authors developed high-throughput, solid-phase protease activity assays for four of the seven **BoNT** serotypes: A, B, D, and F. Each assay consisted of a cleavable oligopeptide, based on the natural substrate sequence, labeled with fluorescein and covalently attached to maleimide-activated multiwell plates. Solns. of holotoxin or nontoxic catalytic domain of **BoNT** were incubated in substrate-coated wells, with or without test compds., followed by transfer and assay of solubilized product in a multiwell fluorometer. Routine toxin concns. ranged from 10 to 100 ng/mL, but concns. as low as 2 ng/mL gave reproducible signals. The fluorescence assays were selective, gave very low background readings, and were stable upon prolonged storage. Using the nontoxic catalytic domain of **BoNT** A, the authors detd. the relative inhibitory potencies of a family of structurally related pseudotripeptide compds. Unlike previous methods, the authors' assays did not employ antibodies or reverse-phase extn. steps, only well-to-well transfers, and were easily adapted to a high-throughput automated environment. (c) 2001 Academic Press.

IT **381670-91-3D**, immobilized; fluorescein labeled
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(substrate; high-throughput solid-phase fluorometric assays for metalloproteinase activities of **botulinum** neurotoxins A, B, D

and F and inhibitory potencies of pseudotripeptides with **botulin** A)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:185784 CAPLUS
DOCUMENT NUMBER: 134:232968
TITLE: Protease-resistant SNARE mutants and the uses thereof in rescue of cellular exocytosis for clostridial neurotoxin-poisoned patients
INVENTOR(S): Dolly, James Oliver; O'Sullivan, Gregory A.; Mohammed, Nadiem; Foran, Patrick G.
PATENT ASSIGNEE(S): Imperial College Innovations Limited, UK
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018038	A2	20010315	WO 2000-GB3196	20000818
WO 2001018038	A3	20011011		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1210444	A2	20020605	EP 2000-956652	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-149993P P 19990820
WO 2000-GB3196 W 20000818

AB A method of treating a patient suffering from poisoning by clostridial toxin wherein a SNARE (sol. (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor) that is resistant to proteolysis by the said clostridial toxin (toxin-resistant SNARE) and/or is capable of inhibiting the clostridial toxin is supplied to a cell of the patient. The SNARE that is resistant to proteolysis may be, synaptosomal-assocd. polypeptide of 25 kDA (SNAP-25). The SNAP-25 is preferably resistant to proteolysis by **BoNT**/A, **BoNT**/E and **BoNT**/C. A method of treating a patient in need of inhibition of SNARE-dependent exocytosis from a cell capable of performing SNARE-dependent exocytosis wherein a deriv. (inhibitory SNARE) that is capable of inhibiting SNARE-dependent exocytosis is supplied to the said cell of the patient. The inhibitory SNARE may be a fragment of SNAP-25 that is derivable by cleavage of SNAP-25 by **botulinum** toxin A (**BoNT**/A). The cell may be, for example, a nerve cell, adreno-chromaffin cell or insulin-secreting cell. The SNARE may be supplied to the cell by expressing recombinant polynucleotide construct. The SNARE or construct may be targeted to a nerve cell, by means of an inactive clostridial neurotoxin. The SNARE may be expressed under the target cell-specific promoter.

IT **126880-89-5**, Protein SNAP 25 (mouse clone p8.52/p8.51 synaptosome-associated reduced) **154768-88-4 329758-74-9**

329764-57-0
RL: PRP (Properties)
(unclaimed protein sequence; protease-resistant SNARE mutants and the uses thereof in rescue of cellular exocytosis for clostridial neurotoxin-poisoned patients)

L7 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:7597 CAPLUS
DOCUMENT NUMBER: 134:91082
TITLE: Peptide inhibitors of neurotransmitter secretion by neuronal cells
INVENTOR(S): Montal, Mauricio; Canaves, Jaume M.; Ferrer-Monteil, Antonio V.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 23 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6169074	B1	20010102	US 1997-819286	19970318

PRIORITY APPLN. INFO.: US 1996-13599P P 19960318

AB The invention consists of peptides which inhibit the secretion of neurotransmitters from synaptic vesicles. The peptides of the invention are believed to mimic the activity of neurotoxins produced by Clostridium **botulinum** and tetani (including **botulinum** serotypes A, B, C, D, E, F and G). Structurally, the peptides are comprised of amino acid fragments from the substrate binding domains selected from three proteins which bind to form a receptor for docking of synaptic vesicles to the plasma membranes of neuronal cells; i.e., SNAP-25, VAMP-2 and syntaxin. Certain of the inventive peptides exhibit strong inhibitory activity; e.g., 50% or greater decline in neurotransmitter release is obtained at even nanomolar concns. The peptides are suited for use as substitutes for Clostridium neurotoxins in clin. applications and in compds. for targeted delivery of drugs into neural cells.

IT **169265-36-5 196928-77-5 197099-52-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Clostridium neurotoxin-mimicking peptide inhibitors of neurotransmitter secretion by neuronal cells)

IT **126880-89-5**, Protein SNAP 25 (mouse clone p8.52/p8.51 synaptosome-associated reduced)
RL: PRP (Properties)
(unclaimed protein sequence; peptide inhibitors of neurotransmitter secretion by neuronal cells)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:132673 CAPLUS
DOCUMENT NUMBER: 132:304502
TITLE: Peptides that mimic the carboxy-terminal domain of SNAP-25 block acetylcholine release at an Aplysia synapse
AUTHOR(S): Apland, J. P.; Biser, J. A.; Adler, M.; Ferrer-Montiel, A. V.; Montal, M.; Filbert, M. G.
CORPORATE SOURCE: Neurotoxicology Branch, US Army Medical Research

Institute of Chemical Defense, Aberdeen Proving Ground, MD, 21010-5400, USA
SOURCE: Journal of Applied Toxicology (1999), 19(Suppl. 1), S23-S26
CODEN: JJATDK; ISSN: 0260-437X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Botulinum** neurotoxin serotypes A and E (**BoNT**/A and **BoNT**/E) block neurotransmitter release, presumably by cleaving SNAP-25, a protein involved in docking of synaptic vesicles with the presynaptic plasma membrane. Three excitation-secretion uncoupling peptides (ESUPs), which mimic the carboxy-terminal domain of SNAP-25 and span or adjoin the cleavage sites for **BoNT**/A and **BoNT**/E, also inhibit transmitter release from permeabilized bovine chromaffin cells. In this study, these peptides were tested for effects on acetylcholine (ACh) release at an identified cholinergic synapse in isolated buccal ganglia of Aplysia californica. The presynaptic neuron was stimulated elec. to elicit action potentials. The postsynaptic neuron was voltage-clamped, and evoked inhibitory postsynaptic currents (IPSCs) were recorded. The ESUPs were pressure-injected into the presynaptic neuron, and their effects on the amplitude of the IPSCs were studied. Acetylcholine release from presynaptic cells, as measured by IPSC amplitudes, was gradually inhibited by the ESUPs. All three peptides caused .apprx.40% redn. in IPSC amplitude in 2 h. Random-sequence peptides of the same amino acid compn. had no effect. Injection of **BoNT**/E, in contrast, caused .apprx.50% redn. in IPSC amplitude in 30 min and almost complete inhibition in 2 h. These results are the first demonstration that ESUPs block neuronal cholinergic synaptic transmission. They are consistent with the concept that ESUPs compete with the intact SNAP-25 for binding with other fusion proteins, thus inhibiting stimulus-evoked exocytosis of neurotransmitter.

IT **169265-36-5 196928-77-5**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(peptides that mimic carboxy-terminal domain of SNAP-25 block acetylcholine release at Aplysia synapse)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:655992 CAPLUS
DOCUMENT NUMBER: 131:268976
TITLE: Assay for the proteolytic activity of **botulin** neurotoxin type A from Clostridium **botulinum**, substrate requirements and activation by serum albumin
INVENTOR(S): Schmidt, James J.; Bostian, Karen A.
PATENT ASSIGNEE(S): United States Dept. of the Army, USA
SOURCE: U.S., 28 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5965699	A	19991012	US 1996-743894	19961106

AB A label-based assay is described, through modifications of peptide substrate structure and derivatization of serum albumin, which can be used to det. proteolytic activity of **botulin** neurotoxin A (botox A)

without sepn. of products. The present invention provides a method for screening compds. for botox A inhibitory or stimulatory activity. Substrate requirements for botox A were also studied.

IT **245360-92-3 245360-93-4 245360-95-6**
245360-96-7 245360-97-8 245360-98-9
245360-99-0 245361-00-6 245361-01-7
245361-02-8 245361-03-9 245361-04-0
245361-05-1 245361-09-5 245361-11-9
245361-13-1 245361-16-4 245361-18-6
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(assay for proteolytic activity of **botulin** neurotoxin A from Clostridium **botulinum**, substrate requirements and activation by serum albumin)

IT **188591-98-2 188591-99-3 188592-01-0**
188592-02-1 188592-03-2 188592-04-3
188592-05-4 188592-16-7 188592-17-8
188592-18-9 245361-21-1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(assay for proteolytic activity of **botulin** neurotoxin A from Clostridium **botulinum**, substrate requirements and activation by serum albumin)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:636059 CAPLUS
DOCUMENT NUMBER: 131:268231
TITLE: Antibody-based assay for **botulinum** and tetanus neurotoxins
INVENTOR(S): Shone, Clifford Charles; Hallis, Bassam; James, Benjamin Arthur Frederick; Quinn, Conrad Padraig
PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: U.S., 21 pp., Cont.-in-part of Appl. No. PCT/GB95/01279.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5962637	A	19991005	US 1996-760001	19961203
WO 9533850	A1	19951214	WO 1995-GB1279	19950602
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6043042	A	20000328	US 1998-15960	19980130
US 6337386	B1	20020108	US 2000-534572	20000327

PRIORITY APPLN. INFO.:
GB 1994-11138 A 19940603
WO 1995-GB1279 A2 19950602
US 1996-760001 A3 19961203
US 1998-15960 A1 19980130

AB The invention provides an antibody-based assay for toxins having peptidase activity, and in particular, this invention relates to assays for **botulinum** and tetanus neurotoxins. The invention comprises the steps of: (a) combining a test compd. with a substrate and with antibody, wherein the substrate has a cleavage site for the toxin and when cleaved by toxin forms a product, and wherein the antibody binds to the product but not to the substrate; and (b) testing for the presence of antibody bound to the product, which product is attached to a solid phase assay

component. Preferably, the substrate is a peptide or a protein which is cleaved by the toxin to generate new peptides have N- and C-terminal ends. In addn., the target peptide is preferably selected from the group VAMP, SNAP-25, and syntaxin, and it may also be from analogs, isoforms, and/or fragments thereof. Furthermore, the assay is capable of distinguishing between active and inactive toxin present within the sample, since inactive toxin will have reduced or no activity.

IT **173080-83-6**
RL: PRP (Properties)
(unclaimed protein sequence; antibody-based assay for **botulinum** and tetanus neurotoxins)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:630583 CAPLUS
DOCUMENT NUMBER: 130:21584
TITLE: The 26-mer peptide released from SNAP-25 cleavage by **botulinum** neurotoxin E inhibits vesicle docking
AUTHOR(S): Ferrer-Montiel, Antonio V.; Gutierrez, Luis M.; Apland, James P.; Canaves, Jaume M.; Gil, Anabel; Viniegra, Salvador; Biser, Jennifer A.; Adler, Michael; Montal, Mauricio
CORPORATE SOURCE: Department of Biology, University of California San Diego, La Jolla, CA, 92093-0366, USA
SOURCE: FEBS Letters (1998), 435(1), 84-88
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Botulinum** neurotoxin E (**BoNT** E) cleaves SNAP-25 at the C-terminal domain releasing a 26-mer peptide. This peptide product may act as an excitation-secretion uncoupling peptide (ESUP) to inhibit vesicle fusion and thus contribute to the efficacy of **BoNT** E in disabling neurosecretion. We have addressed this question using a synthetic 26-mer peptide which mimics the amino acid sequence of the naturally released peptide, and is hereafter denoted as ESUP E. This synthetic peptide is a potent inhibitor of Ca2+-evoked exocytosis in permeabilized chromaffin cells and reduces neurotransmitter release from identified cholinergic synapses in in vitro buccal ganglia of Aplysia californica. In chromaffin cells, both ESUP E and **BoNT** E abrogate the slow component of secretion without affecting the fast, Ca2+-mediated fusion event. Anal. of immunoppts. of the synaptic ternary complex involving SNAP-25, VAMP and syntaxin demonstrates that ESUP E interferes with the assembly of the docking complex. Thus, the efficacy of **BoNTs** as inhibitors of neurosecretion may arise from the synergistic action of cleaving the substrate and releasing peptide products that disable the fusion process by blocking specific steps of the exocytotic cascade.

IT **196928-77-5**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(SNAP-25 peptide ESUP E; 26-mer peptide released from SNAP-25 cleavage by **botulinum** neurotoxin E which inhibits synaptic vesicle docking)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:630507 CAPLUS
DOCUMENT NUMBER: 130:34875
TITLE: Type A **botulinum** neurotoxin proteolytic activity: development of competitive inhibitors and implications for substrate specificity at the S1' binding subsite
AUTHOR(S): Schmidt, James J.; Stafford, Robert G.; Bostian, Karen A.
CORPORATE SOURCE: Toxinology Division, United States Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD, 21702-5011, USA
SOURCE: FEBS Letters (1998), 435(1), 61-64
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Type A **botulinum** neurotoxin (botox A) is a zinc metalloprotease that cleaves only one peptide bond in the synaptosomal protein, SNAP-25. Single-residue changes in a 17-residue substrate peptide were used to develop the first specific, competitive inhibitors of its proteolytic activity. Substrate analog peptides with P4, P3, P2' or P3' cysteine were readily hydrolyzed by the toxin, but those with P1 or P2 cysteine were not cleaved and were inhibitors. Peptides with either D- or L-cysteine as the N-terminus, followed by the last six residues of the substrate, were the most effective inhibitors, each with a Ki value of 2 .mu.M. Elimination of the cysteine sulfhydryl group yielded much less effective inhibitors, suggesting that inhibition was primarily due to binding of the active-site zinc by the sulfhydryl group. Botox A displayed an unusual requirement for arginine as the P1' inhibitor residue, demonstrating that the S1' binding subsite of botox A is dissimilar to those of most other zinc metalloproteases. This characteristic is an important element in shaping the substrate specificity of botox A.

IT **216568-37-5 216568-38-6 216568-39-7**
216568-46-6
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors and substrates of botox A, a type A **botulinum** neurotoxin with proteolytic activity)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:640559 CAPLUS
DOCUMENT NUMBER: 127:298730
TITLE: Peptide neurotoxin analog inhibitors of neurotransmitter secretion by neuronal cells for neural targeting of drugs
INVENTOR(S): Montal, Mauricio
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734620	A1	19970925	WO 1997 US4393	19970319

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,

LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9723348 A1 19971010 AU 1997-23348 19970318
PRIORITY APPLN. INFO.: US 1996-13599P P 19960318
WO 1997-US4393 W 19970318

AB The invention consists of peptides which inhibit the secretion of neurotransmitters from synaptic vesicles. The peptides of the invention are believed to mimic the activity of neurotoxins produced by Clostridium **botulinum** and C. tetani (including **botulinum** serotypes A, B, C, D, E, F and G). Structurally, the peptides are comprised of amino acid fragments from the substrate binding domains selected from three proteins which bind to form a receptor for docking of synaptic vesicles to the plasma membranes of neuronal cells; i.e., SNAP-25, VAMP-2 and syntaxin. Certain of the inventive peptides exhibit strong inhibitory activity; e.g. 50 % or greater decline in neurotransmitter release is obtained at even nanomolar concns. The peptides are suited for use as substitutes for Clostridium neurotoxins in clin. applications and in compds. for targeted delivery of drugs into neural cells.

IT **169265-36-5 196928-77-5 197099-52-8**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(peptide neurotoxin analog inhibitors of neurotransmitter secretion by neuronal cells for neural targeting of drugs)

L7 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:527491 CAPLUS
DOCUMENT NUMBER: 127:188490
TITLE: Blockade of ACh release at a synapse in Aplysia by a peptide that mimics the carboxy-terminal domain of SNAP-25
AUTHOR(S): Apland, J. P.; Filbert, M. G.; Adler, M.; Ferrer-Montiel, A. V.; Montal, M.
CORPORATE SOURCE: Neurotoxicology Branch, U. S. Army Medical Research Institute Chemical Defense, Aberdeen Proving Ground, MD, 21010-5425, USA
SOURCE: Medical Defense Bioscience Review, Proceedings, Baltimore, May 12-16, 1996 (1996), Volume 3, 1434-1439. National Technical Information Service: Springfield, Va.
CODEN: 64UTAN
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Neurotransmitter exocytosis is preceded by docking of synaptic vesicles at release sites on the presynaptic membrane. SNAP-25 (synaptosomal-assocd. membrane protein of 25 kDa) is one of several proteins forming the fusion complex at the release sites. **Botulinum** neurotoxins A and E block neurotransmitter release by cleaving SNAP-25. The SNAP-25 C-terminal 20-amino acid peptide (named ESUP, for excitation-secretion uncoupling peptide) was recently shown by L.M. Gutierrez, et al. (1995) to inhibit transmitter release from permeabilized bovine chromaffin cells. The effect of this peptide on ACh release at an identified cholinergic synapse of Aplysia neurons was investigated in preliminary expts. in the authors' lab. Recordings were obtained from isolated buccal ganglia of Aplysia. The presynaptic neuron was current-clamped and stimulated elec. at 0.017 Hz or 0.1 Hz to elicit action potentials. The postsynaptic neuron was voltage-clamped, and evoked inhibitory postsynaptic currents

(IPSCs) were recorded. ESUP was pressure-injected into the presynaptic neuron, and its effect on the amplitude of the IPSCs was studied. ACh release from presynaptic cells, as measured by the amplitudes of IPSCs, was consistently inhibited. The inhibition was gradual, requiring 1-3 h to effect a 50-60% redn. of IPSC amplitude. A random-sequence peptide of the same amino acid compn. had no effect. Apparently, ESUP competes with the intact SNAP-25 for binding with other fusion proteins, thus inhibiting exocytosis of neurotransmitter. This effect may account, in part, for **botulinum** toxin-induced inhibition of transmitter release.

IT **169265-36-5**, Excitation-secretion uncoupling peptide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(blockade of acetylcholine release at synapse in Aplysia by peptide that mimics C-terminal domain of SNAP-25)

L7 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:152896 CAPLUS
DOCUMENT NUMBER: 126:235112
TITLE: Endoproteinase activity of type A **botulinum** neurotoxin: substrate requirements and activation by serum albumin
AUTHOR(S): Schmidt, James J.; Bostian, Karen A.
CORPORATE SOURCE: Toxinology Division, U.S. Army Medical Res. Institute Infectious Diseases, Frederidck, MD, 21702-5011, USA
SOURCE: Journal of Protein Chemistry (1997), 16(1), 19-26
CODEN: JPCHD2; ISSN: 0277-8033
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Type A **botulinum** neurotoxin, a zinc-dependent endoproteinase that selectively cleaves the neuronal protein SNAP-25, can also cleave relatively short peptides. We found that bovine and other serum albumins stimulated the type A-catalyzed hydrolysis of synthetic peptide substrates, through a direct effect on the kinetic consts. of the reaction. Furthermore, with bovine serum albumin in the assays, the optimum substrate size was 16 residues (11 on the amino-terminal side of the cleavage site and 5 on the carboxy-terminal side). To further investigate the catalytic requirements of the neurotoxin, peptides were synthesized with various amino acid substitutions at the P5 through P5' substrate sites. Changes at all of these locations affected values for both kcat and Km. Substitutions at the P2, P1', and P2' sites had more pronounced effects on hydrolysis rates than did substitutions at the P1 site. Enzyme-substrate interactions at the P3' threonine probably involved the side-chain Me group rather than the hydroxyl group. Replacing the P2' alanine with leucine eliminated detectable hydrolysis, but not binding, since this peptide was an inhibitor. A neg. charged residue was preferred at P5, but not at P4. The data indicate that type A **botulinum** neurotoxin has an extended substrate recognition region and a requirement for arginine as the P1' residue.

IT **188591-98-2 188591-99-3 188592-00-9**
188592-01-0 188592-02-1 188592-03-2
188592-04-3 188592-05-4 188592-16-7
188592-17-8 188592-18-9
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(endoproteinase activity of type A **botulinum** neurotoxin, substrate requirements and activation by serum albumin)

L7 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:97334 CAPLUS
DOCUMENT NUMBER: 126:197791

TITLE: A peptide that mimics the C-terminal sequence of SNAP-25 inhibits secretory vesicle docking in chromaffin cells
AUTHOR(S): Gutierrez, Luis M.; Viniegra, Salvador; Rueda, Joaquin; Ferrer-Montiel, Antonio V.; Canaves, Jaume M.; Montal, Mauricio
CORPORATE SOURCE: Instituto de Neurociencias and Facultad de Medicina, Universidad de Alicante, Alicante, 03080, Spain
SOURCE: Journal of Biological Chemistry (1997), 272(5), 2634-2639
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Excitation-secretion uncoupling peptides (ESUPs) are inhibitors of Ca2+-dependent exocytosis in neural and endocrine cells. Their mechanism of action, however, remains elusive. We report that ESUP-A, a 20-mer peptide patterned after the C terminus of SNAP-25 (synaptosomal assocd. protein of 25 kDa) and contg. the cleavage sequence for **botulinum** neurotoxin A (**BoNT** A), abrogates the slow, ATP-dependent component of the exocytotic pathway, without affecting the fast, ATP-independent, Ca2+-mediated fusion event. Ultrastructural anal. indicates that ESUP-A induces a drastic accumulation of dense-core vesicles near the plasma membrane, mimicking the effect of **BoNT** A. Together, these findings argue in favor of the notion that ESUP-A inhibits ATP-primed exocytosis by blocking vesicle docking. Identification of blocking peptides which mimic sequences that bind to complementary partner domains on interacting proteins of the exocytotic machinery provides new pharmacol. tools to dissect the mol. and mechanistic details of neurosecretion. Our findings may assist in developing ESUPs as substitute drugs to **BoNTs** for the treatment of spasmodic disorders.

IT **169265-36-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence of; SNAP-25 C-terminal sequence-like peptide ESUP-A inhibits ATP-dependent secretory vesicle docking in bovine adrenal chromaffin cells)

L7 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:87093 CAPLUS
DOCUMENT NUMBER: 124:109558
TITLE: Toxin assay
INVENTOR(S): Shone, Clifford Charles; Hallis, Bassam; James, Benjamin Arthur Frederick; Quinn, Conrad Padraig
PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533850	A1	19951214	WO 1995-GB1279	19950602
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9526240	A1	19960104	AU 1995-26240	19950602
AU 687564	B2	19980226		

EP 763131	A1	19970319	EP 1995-921033	19950602
EP 763131	B1	19990825		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL, SE				
JP 10504801	T2	19980512	JP 1995-500544	19950602
AT 183779	E	19990915	AT 1995-921033	19950602
US 5962637	A	19991005	US 1996-760001	19961203
US 6043042	A	20000328	US 1998-15960	19980130
US 6337386	B1	20020108	US 2000-534572	20000327

PRIORITY APPLN. INFO.: GB 1994-11138 A 19940603
WO 1995-GB1279 W 19950602
US 1996-760001 A3 19961203
US 1998-15960 A1 19980130

AB A toxin assay that uses a substrate for cleavage by the toxin and antibodies that do not recognize the substrate but recognize and bind to the product of cleavage of the substrate by the toxin. The substrate can be a nerve cell peptide when the assay is for **botulinum** toxin or tetanus toxin.

IT **173080-83-6**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(substrate; tetanus and **botulinum** toxin assay using peptide substrates and antibodies)

L7 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:19380 CAPLUS
DOCUMENT NUMBER: 124:167929
TITLE: Proteolysis of synthetic peptides by type A **botulinum** neurotoxin
AUTHOR(S): Schmidt, James J.; Bostian, Karen A.
CORPORATE SOURCE: U.S. Army Medical Res. Inst. of Infectious Diseases, Fort Detrick, Frederick, MD, 21702-5011, USA
SOURCE: Journal of Protein Chemistry (1995), 14(8), 703-8
CODEN: JPCHD2; ISSN: 0277-8033
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Type A **botulinum** neurotoxin catalyzed the hydrolysis of synthetic peptides based on the sequence of the 25 kDa synaptosomal protein SNAP-25. In each peptide, the toxin cleaved at a single glutaminyl-arginine bond corresponding to residues 197 and 198 of SNAP-25, confirming earlier reports on the enzymic specificity of the toxin in synaptosomal prepns. Metal chelators inhibited catalysis, consistent with a metalloprotease activity. In contrast to tetanus toxin and other **botulinum** toxin serotypes, type A toxin hydrolyzed relatively short, 17-to 20-residue peptides. In the substrates, SNAP-25 residue 202 and one or more of residues 197-191 were required for efficient hydrolysis, but residues 167-186 and 203-206 were not. The highest rates of hydrolysis were found when the C-terminal residues of the peptides were amidated.

IT **169265-36-5 172486-01-0 172486-02-1**
172486-03-2 172486-04-3 172486-05-4
172486-06-5 173762-25-9
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proteolysis of synthetic peptides by type A **botulinum** neurotoxin)

=> file home
FILE 'HOME' ENTERED AT 16:11:07 ON 03 DEC 2002